

Ward 10_658121- - History

=> d his ful

(FILE 'HOME' ENTERED AT 10:07:56 ON 16 MAY 2006)

FILE 'REGISTRY' ENTERED AT 10:08:15 ON 16 MAY 2006

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L1      STR
L3      570 SEA SSS FUL L1

FILE 'HCAPLUS' ENTERED AT 10:10:55 ON 16 MAY 2006
L4      15 SEA ABB=ON PLU=ON L3
        D STAT QUE L4
        D IBIB ABS HITSTR L4 1-15
L5      57 SEA ABB=ON PLU=ON "DESIMONE R W"/AU OR "DESIMONE ROBERT"/AU
        OR ("DESIMONE ROBERT W"/AU OR "DESIMONE ROBERT WALTER JR"/AU)
L6      18 SEA ABB=ON PLU=ON "PIPPIN D A"/AU OR ("PIPPIN DOUGLAS"/AU OR
        "PIPPIN DOUGLAS A"/AU OR "PIPPIN DOUGLAS ANTHONY IRWIN"/AU)
L7      26 SEA ABB=ON PLU=ON ("DARROW J W"/AU OR "DARROW JAMES W"/AU OR
        "DARROW JAMES WILLIAM"/AU)
L8      172 SEA ABB=ON PLU=ON "MITCHELL S"/AU OR "MITCHELL S A"/AU OR
        ("MITCHELL SCOTT"/AU OR "MITCHELL SCOTT A"/AU OR "MITCHELL
        SCOTT ALLAN"/AU)
L9      24 SEA ABB=ON PLU=ON "CURRIE K P M"/AU OR "CURRIE K S"/AU OR
        "CURRIE KEVIN"/AU OR "CURRIE KEVIN S"/AU
L10     1 SEA ABB=ON PLU=ON (L5 AND L6 AND L7 AND L8 AND L9) NOT L4
L11     5 SEA ABB=ON PLU=ON (L5 AND (L6 OR L7 OR L8 OR L9)) NOT L4
L12     3 SEA ABB=ON PLU=ON (L6 AND (L7 OR L8 OR L9)) NOT L4
L13     3 SEA ABB=ON PLU=ON (L7 AND (L8 OR L9)) NOT L4
L14     4 SEA ABB=ON PLU=ON (L8 AND L9) NOT L4
L15     8 SEA ABB=ON PLU=ON L10 OR L11 OR L12 OR L13 OR L14
        D STAT QUE L15 NOS
        D IBIB ABS L15 1-8
L17     50 SEA ABB=ON PLU=ON ((L5 OR L6 OR L7 OR L8 OR L9) AND (?IMIDAZO
        ? OR ?AMINE?)) NOT (L4 OR L15)
L18     40 SEA ABB=ON PLU=ON L17 AND PD=<SEPTEMBER 10, 2003
        D STAT QUE L18 NOS
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FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0

DICTIONARY FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

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*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

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FILE COVERS 1907 - 16 May 2006 VOL 144 ISS 21
FILE LAST UPDATED: 15 May 2006 (20060515/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 10:10:55 ON 16 MAY 2006
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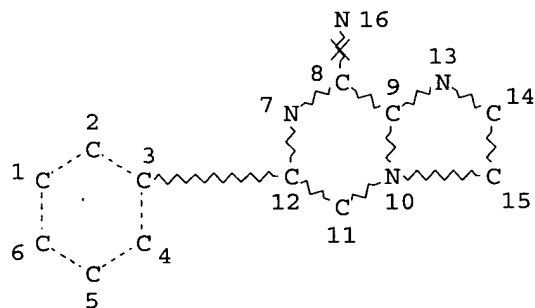
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FILE COVERS 1907 - 16 May 2006 VOL 144 ISS 21
FILE LAST UPDATED: 15 May 2006 (20060515/ED)
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d stat que l4
L1 STR
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NODE ATTRIBUTES:
NSPEC IS RC AT 16
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16
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STEREO ATTRIBUTES: NONE
L3 570 SEA FILE=REGISTRY SSS FUL L1
L4 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
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L4 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004749 HCAPLUS

DOCUMENT NUMBER: 143:306338

TITLE: Preparation of imidazo[1,2-a]pyrazine derivatives as inhibitors of JNK kinases

INVENTOR(S): Birault, Veronique; Harris, Clifford John; Harrison, Stephen Anthony

PATENT ASSIGNEE(S): Biofocus Discovery Limited, UK

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005085252 | A1 | 20050915 | WO 2005-GB842 | 20050304 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

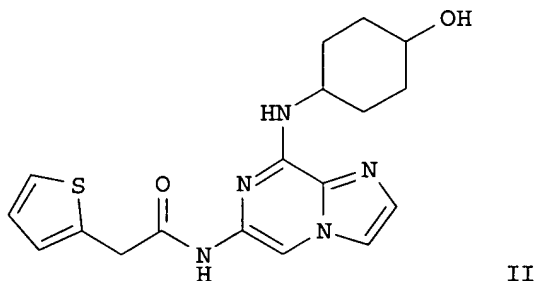
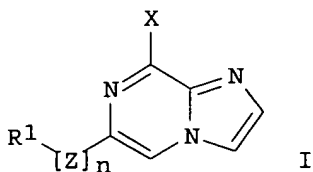
PRIORITY APPLN. INFO.:

GB 2004-4889 A 20040304

GB 2004-26259 A 20041130

OTHER SOURCE(S): MARPAT 143:306338

GI



AB Title compds. I [R1 = (un)substituted heteroaryl, arylalkyl, aryl, etc.; X = NHR2, NR2R3 or OR2; R2 and R3 independently = H, (un)substituted heteroarylalkyl, heteroaryloxy, etc.; Z = NC(O), C(O)N, NS(O)2, etc.; n = 0-1] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of JNK kinases. Thus, e.g., II was prepared by coupling of 6,8-dibromo-imidazo[1,2-a]pyrazine (preparation given) with trans-4-aminocyclohexanol hydrochloride and subsequent amidation with thiophene-2-acetamide. The activity of I was evaluated in JNK screening assays and it was revealed that selected compds. of the invention displayed IC50 values in the range of less than 1 μ M up to 10 μ M. I as inhibitor of JNK kinases should prove useful in the treatment of diseases such as but not limited to rheumatoid arthritis, multiple sclerosis and asthma. Pharmaceutical compns. comprising I are disclosed.

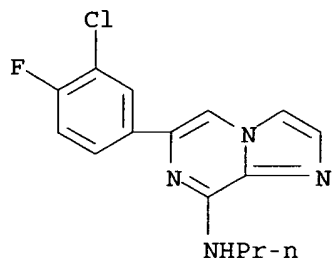
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 864545-96-0P 864546-00-9P 864546-01-0P
 864546-02-1P 864546-03-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

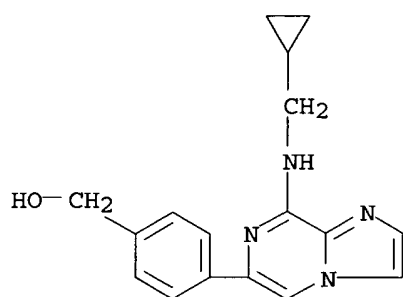
(preparation of imidazo[1,2-a]pyrazine derivs. as inhibitors of JNK kinases)

RN 864545-55-1 HCAPLUS

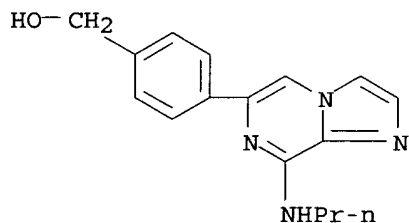
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-chloro-4-fluorophenyl)-N-propyl- (9CI)
 (CA INDEX NAME)



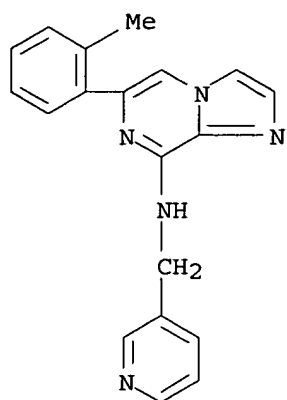
RN 864545-56-2 HCAPLUS
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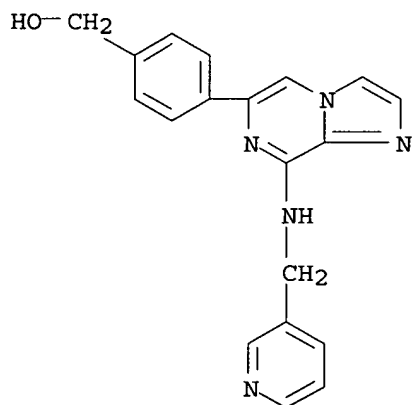
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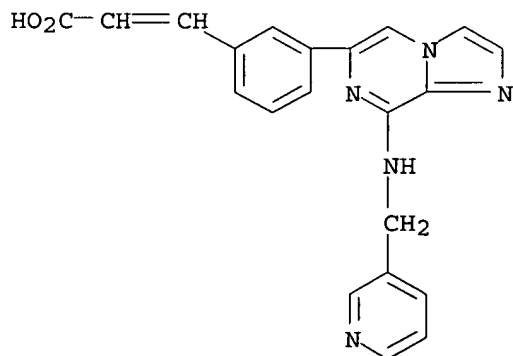
RN 864545-58-4 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-methylphenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 864545-60-8 HCAPLUS
 CN Benzenemethanol, 4-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)

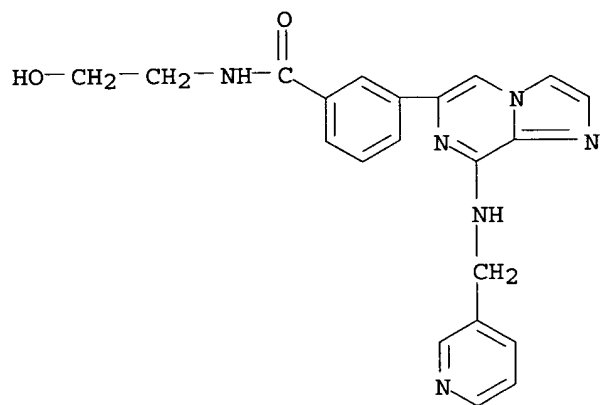


RN 864545-62-0 HCAPLUS
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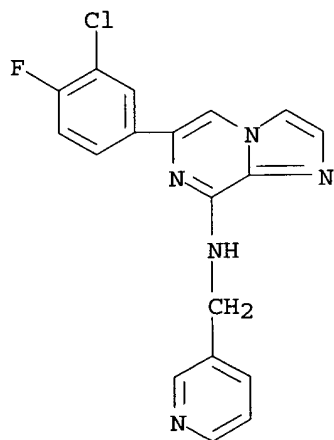
RN 864545-64-2 HCAPLUS

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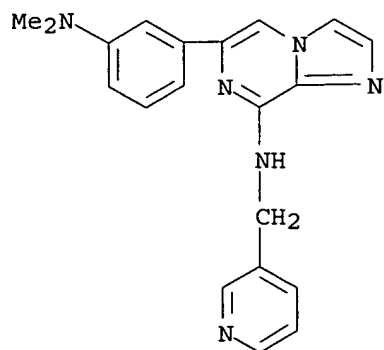
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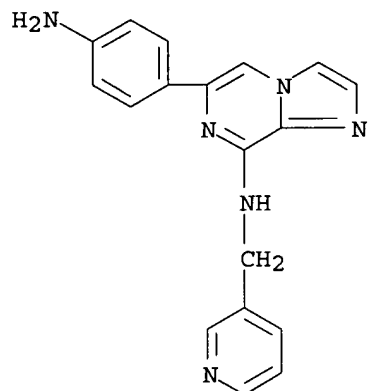
RN 864545-66-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3-(dimethylamino)phenyl]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



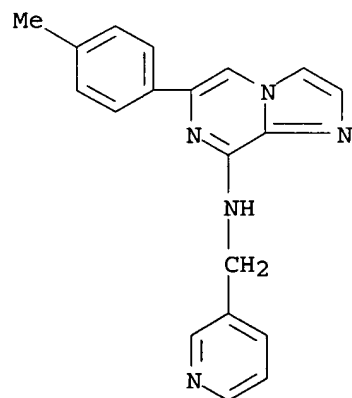
RN 864545-67-5 HCAPLUS

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RN 864545-68-6 HCAPLUS

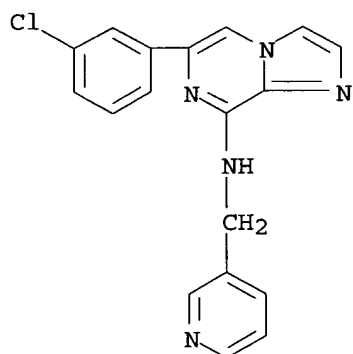
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RN 864545-69-7 HCAPLUS

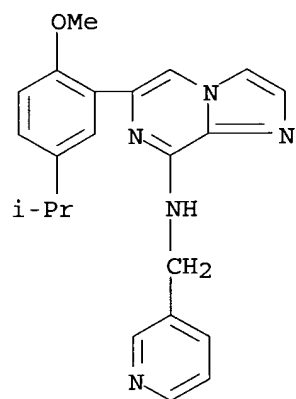
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(9CI) (CA INDEX NAME)



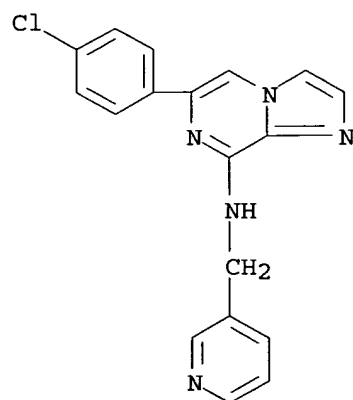
RN 864545-70-0 HCAPLUS

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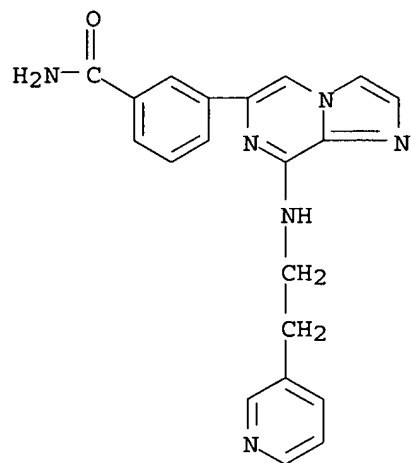
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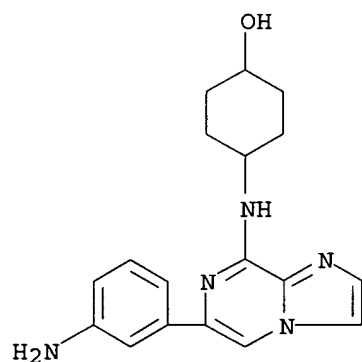
RN 864545-72-2 HCAPLUS

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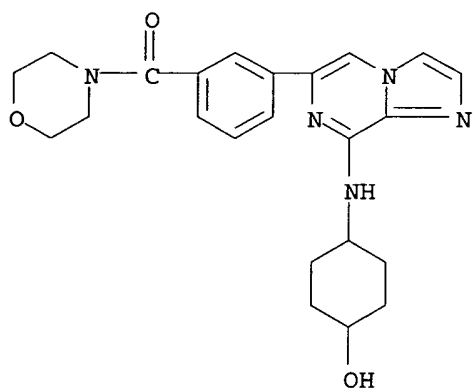
RN 864545-75-5 HCAPLUS

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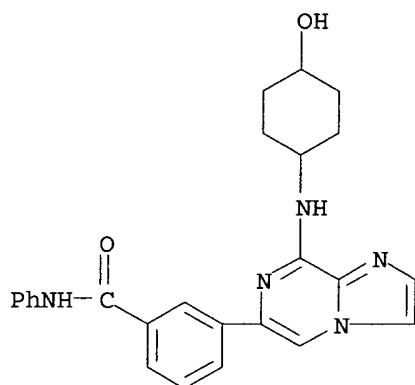
RN 864545-76-6 HCAPLUS

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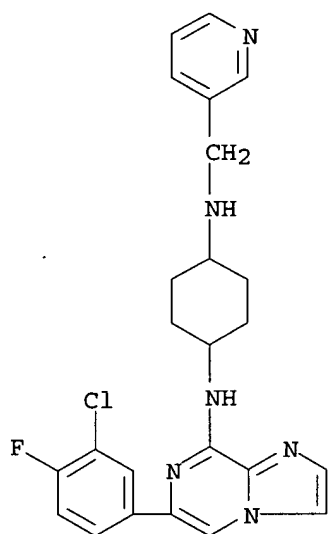
RN 864545-77-7 HCAPLUS

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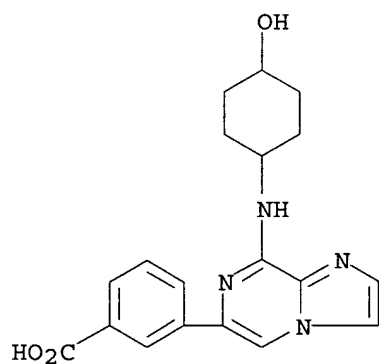
RN 864545-78-8 HCAPLUS

CN 1,4-Cyclohexanediamine, N-[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



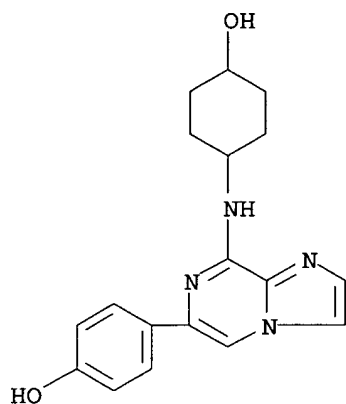
RN 864545-79-9 HCAPLUS

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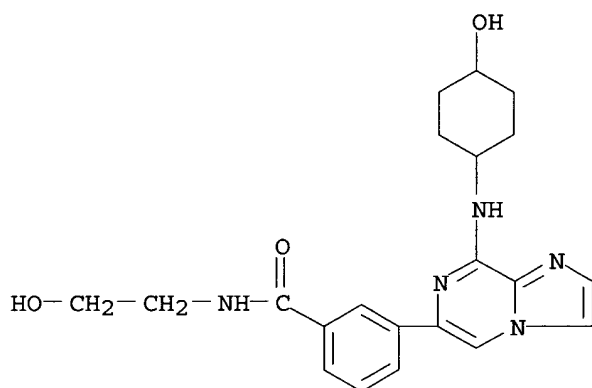
RN 864545-80-2 HCAPLUS

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(9CI) (CA INDEX NAME)



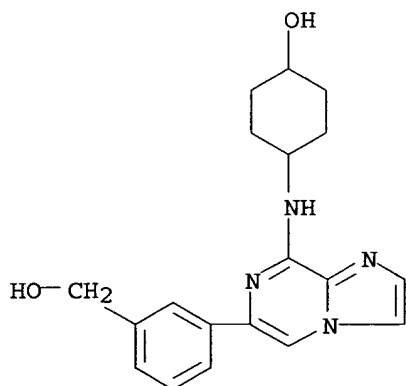
RN 864545-81-3 HCAPLUS

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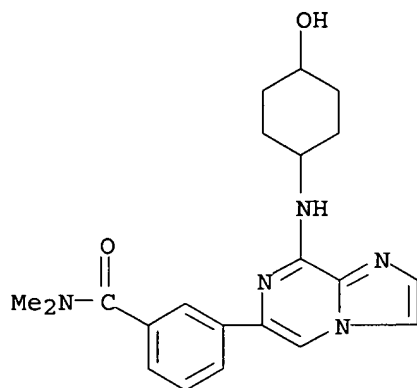
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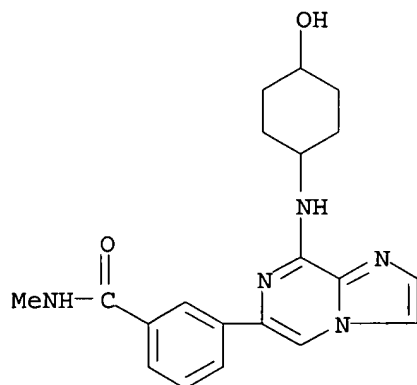
RN 864545-83-5 HCAPLUS

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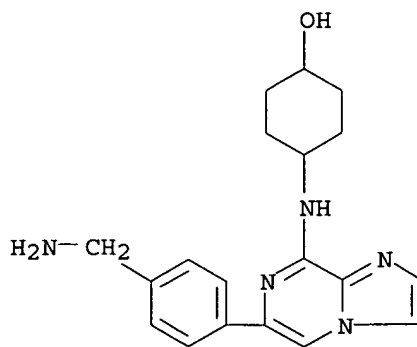
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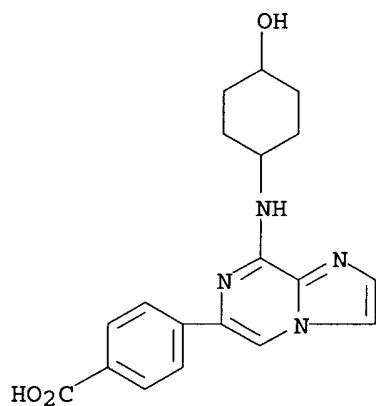
RN 864545-86-8 HCAPLUS

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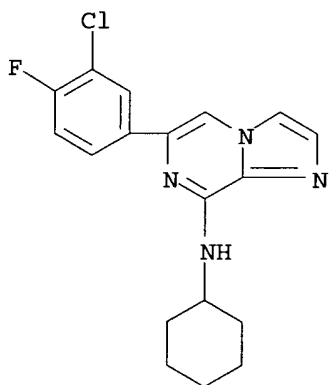
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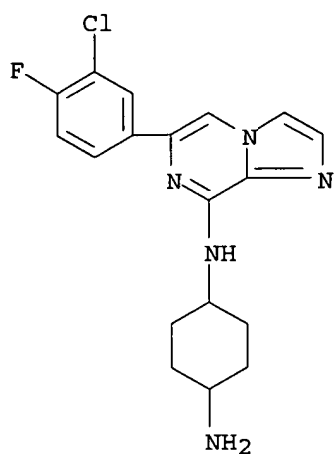
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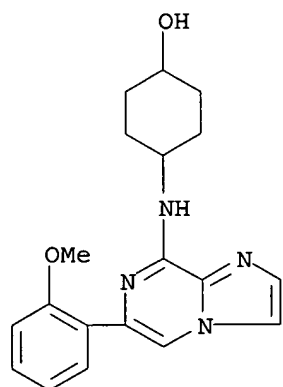


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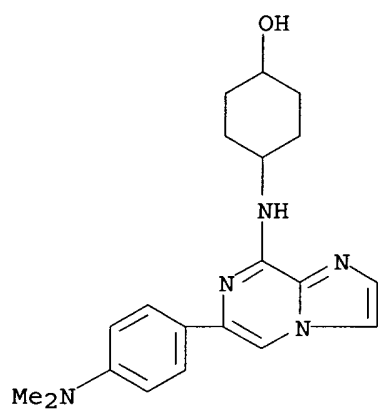
CN 1,4-Cyclohexanediamine, N-[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]- (9CI) (CA INDEX NAME)



RN 864545-91-5 HCAPLUS
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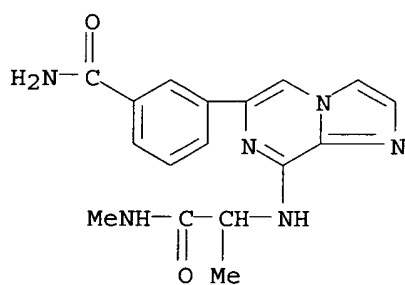


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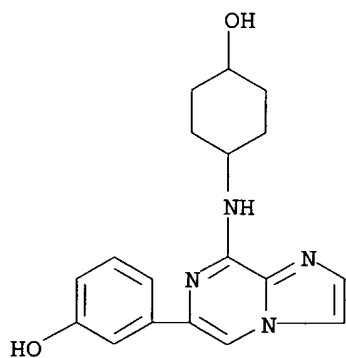
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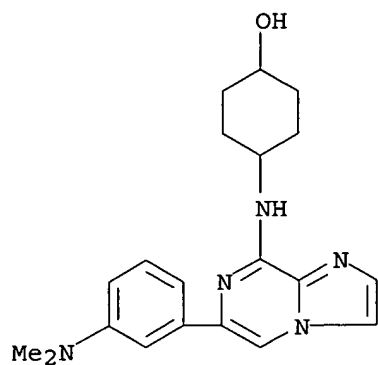
RN 864545-95-9 HCAPLUS

CN Phenol, 3-[8-[[4-hydroxycyclohexyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



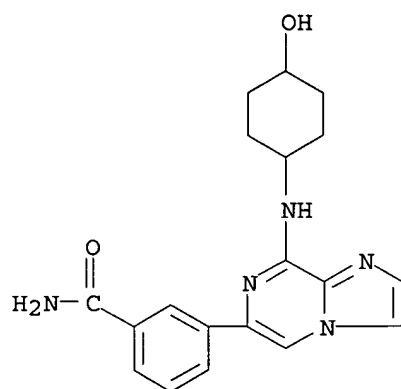
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CN Cyclohexanol, 4-[[6-[3-(dimethylamino)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



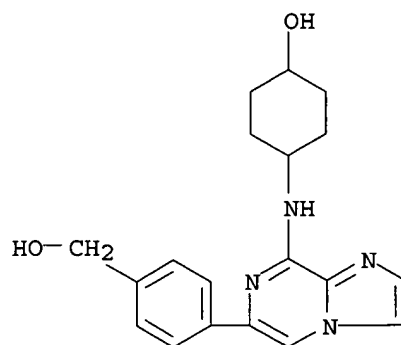
RN 864546-00-9 HCAPLUS

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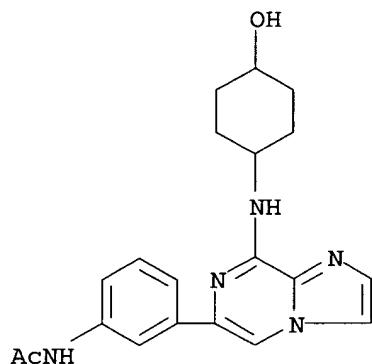
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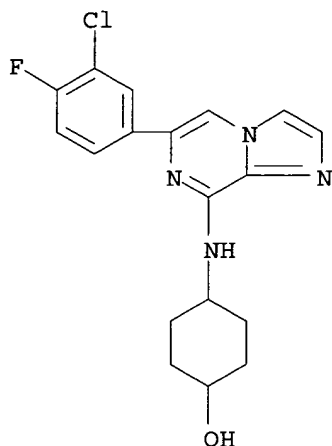
RN 864546-02-1 HCAPLUS

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RN 864546-03-2 HCAPLUS

CN Cyclohexanol, 4-[[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:451386 HCAPLUS

DOCUMENT NUMBER: 143:7734

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as kinase modulators, particularly Btk inhibitors, for treating Btk-related diseases and conditions

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.

PATENT ASSIGNEE(S): Cellular Genomics Inc., USA

SOURCE: PCT Int. Appl., 236 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2005047290 | A2 | 20050526 | WO 2004-US37433 | 20041110 |

WO 2005047290 A3 20050811

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005288295

A1

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US 2004-985023

20041110

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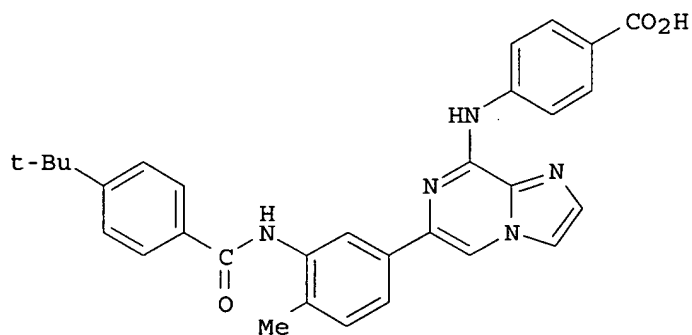
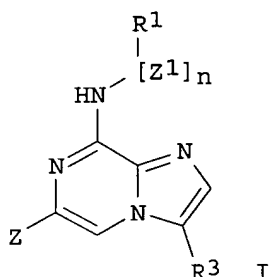
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OTHER SOURCE(S):

MARPAT 143:7734

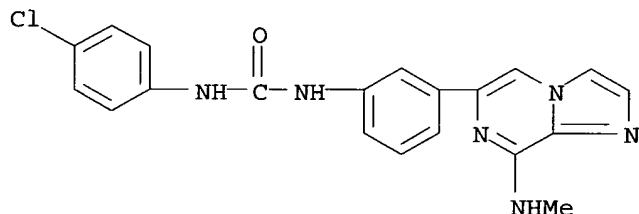
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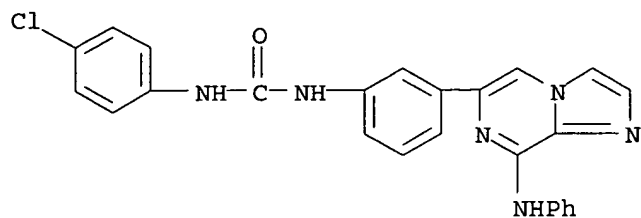
AB The title compds. [I; n = 0-1; Z1 = CO, CONH and derivs., NHSO2 and derivs., etc.; R1 = H, heterocyclo/cyclo/alkyl, alkoxy, (un)substituted Ph, heteroaryl, etc.; Z = -Z2-Q-R2; Z2 = (un)substituted phenylene, pyridylidene, naphthylidene; Q = CO, NHCO and derivs., CH2NH and derivs., SO2NH and derivs., etc.; R2 = (un)substituted heterocyclo/cyclo/alkyl, alkoxy, aryloxy, Ph, heteroaryl; R3 = H, cycloalkyl/heterocyclo/heterocycl oalkylcyclo/alkyl] and their pharmaceutically acceptable salts, hydrates, solvates, crystal forms, diastereomers, and prodrugs, which are of particular utility in the treatment of Btk kinase-implicated disorders, were prepared General methods of preparation were given. All exemplified compds. I such as II were tested in standard AKT-1 kinase assay and standard assay

to evaluate modulation of cell growth in soft agar (using cell lines HCT-15, MiaPaca2, MCF-7 and NIH3T3 clone stably overexpressing transfected myrAkt-1 human gene), and exhibited IC50 of $\leq 25 \mu\text{M}$. I were also tested in standard biochem. and cellular Btk and EphB4 assays; IC50 $< 1 \mu\text{M}$ in the biochem. assays. I and their formulations are useful for treating neoplasm, autoimmune and/or inflammatory conditions.

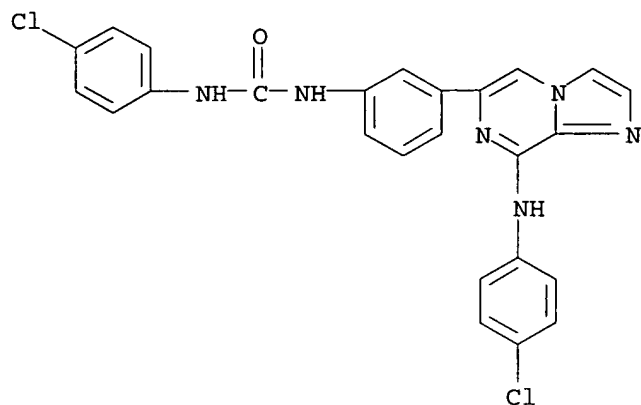
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of imidazo[1,2-a]pyrazin-8-ylamines as kinase, particularly Btk, inhibitors)
 RN 618454-74-3 HCAPLUS
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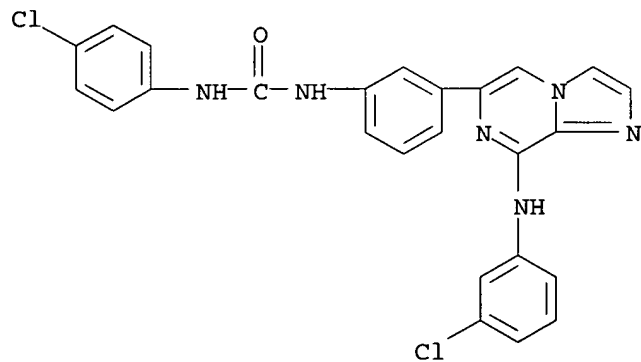
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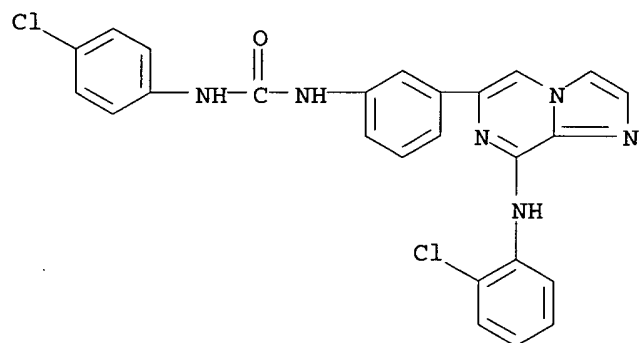
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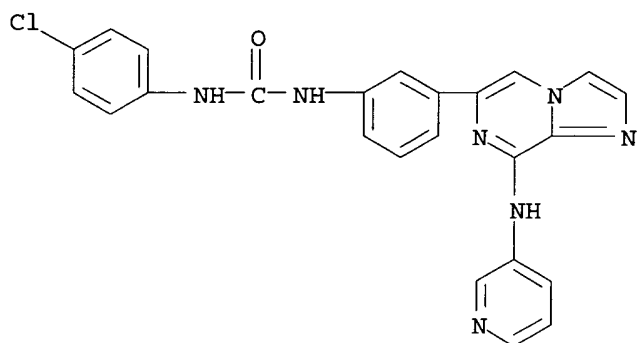
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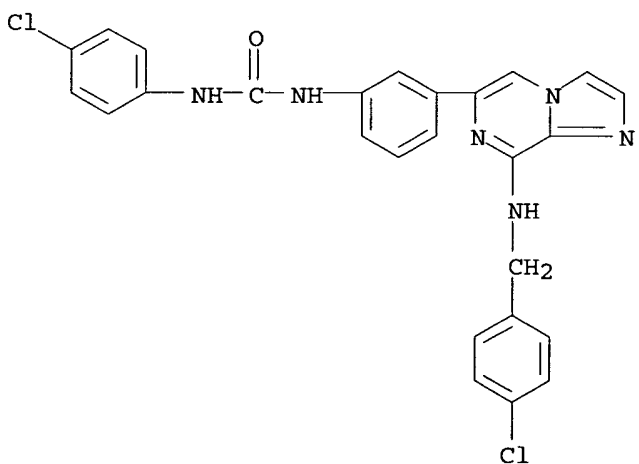
RN 618454-95-8 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



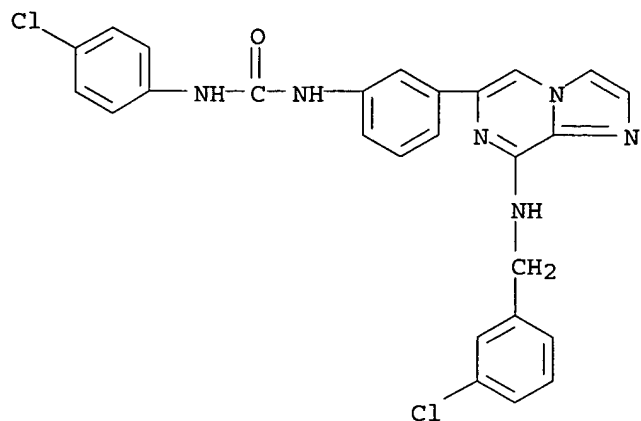
RN 618455-01-9 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(3-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-08-6 HCAPLUS
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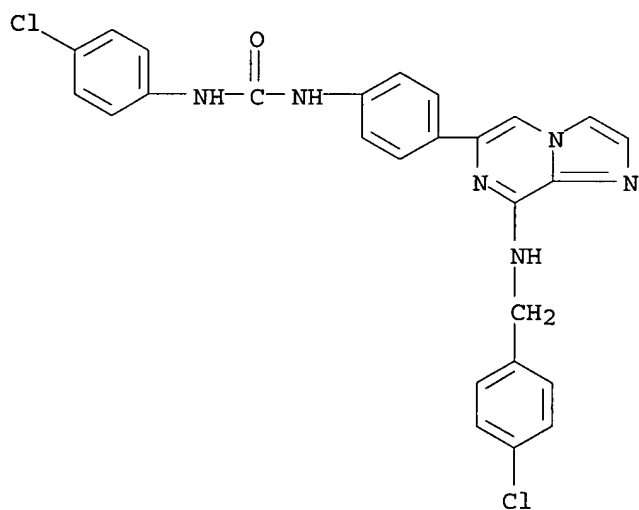


RN 618455-13-3 HCAPLUS
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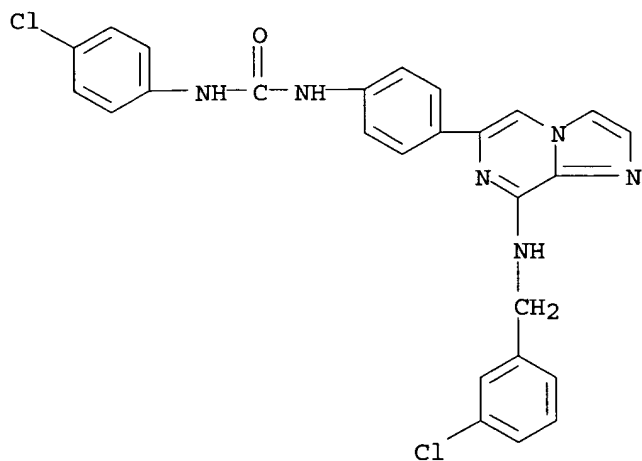
RN 618455-19-9 HCAPLUS

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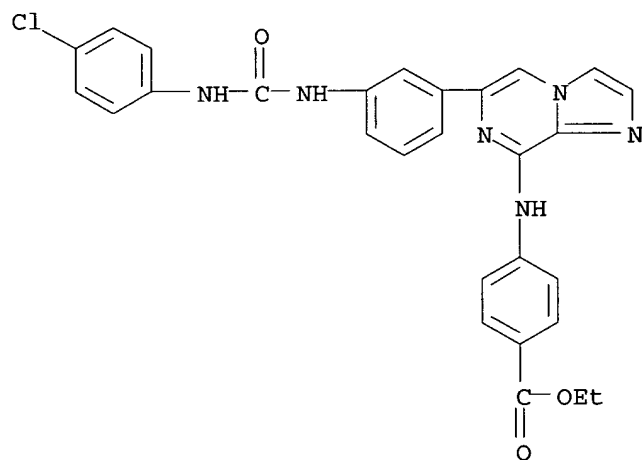
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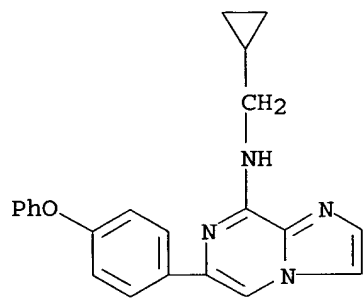
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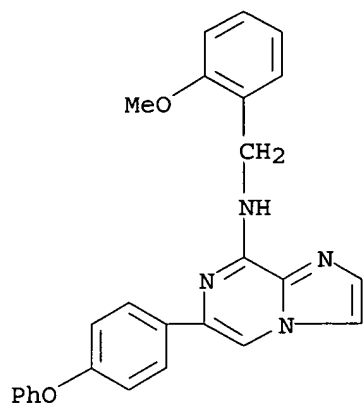


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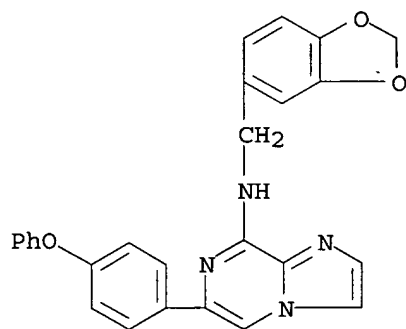
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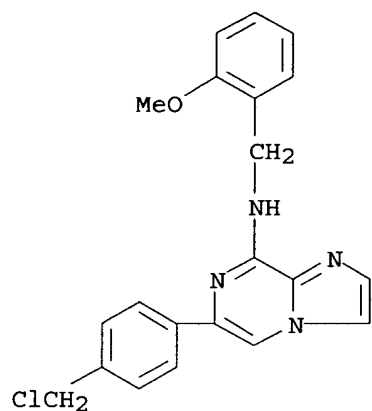
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 CN Imidazo[1,2-a]pyrazin-8-amine, N-[(2-methoxyphenyl)methyl]-6-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 618455-47-3 HCAPLUS
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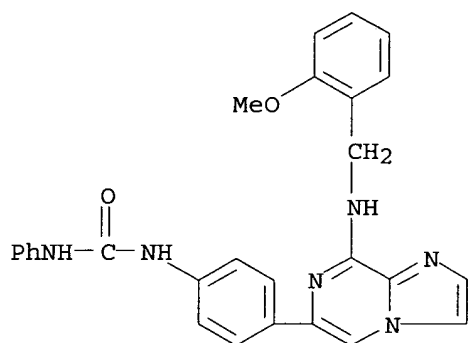


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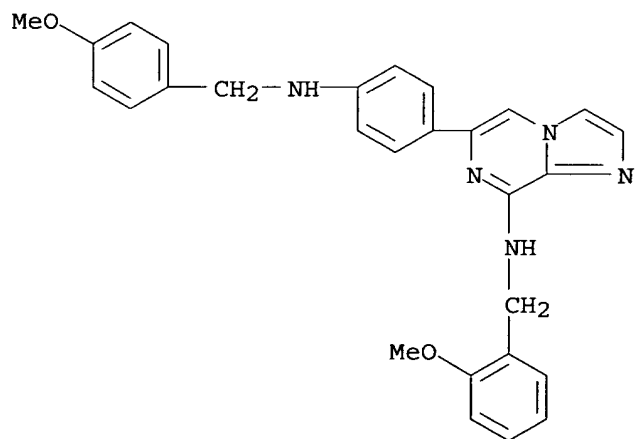
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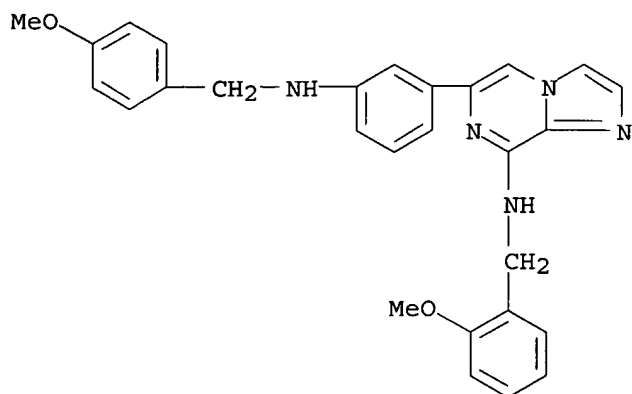
RN 618455-57-5 HCAPLUS

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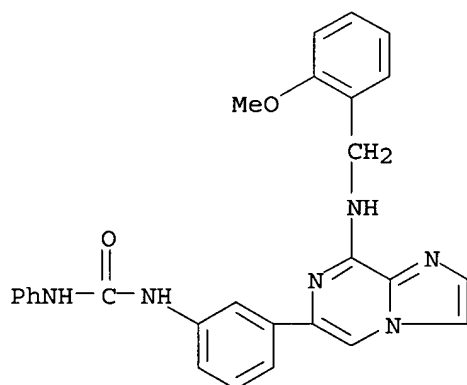
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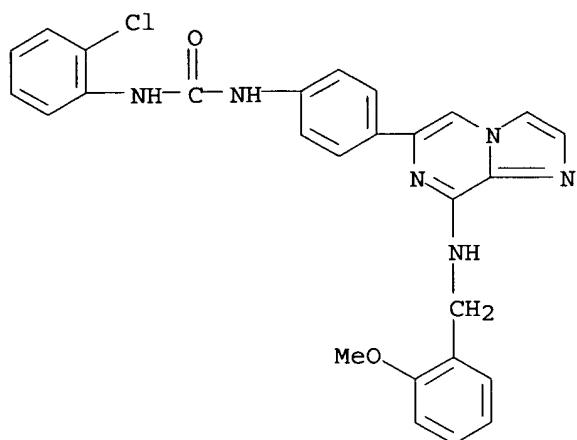
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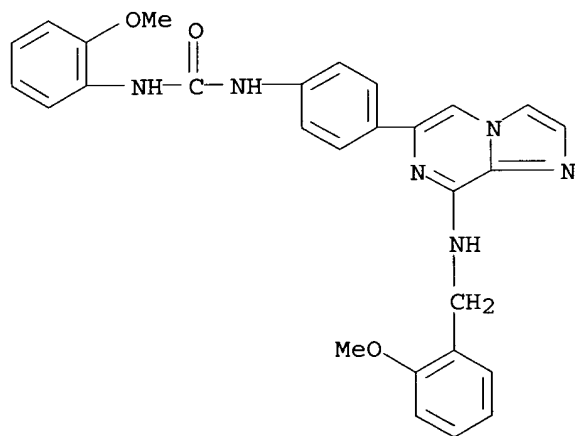
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CN Urea, N-(2-chlorophenyl)-N'-[4-[8-[[[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



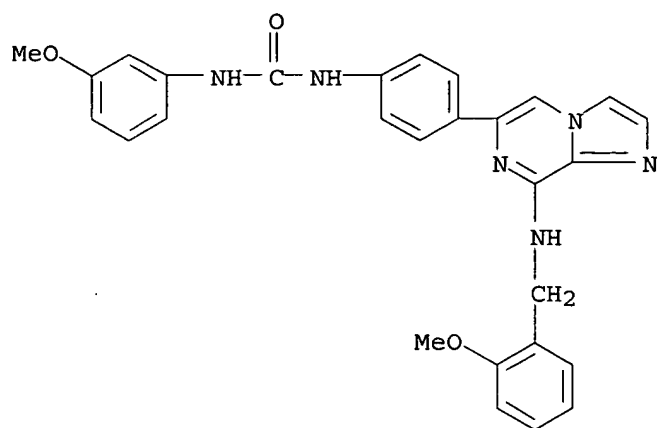
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CN Urea, N-(2-methoxyphenyl)-N'-[4-[8-[[2-methoxyphenyl)methyl]amino]imidazo
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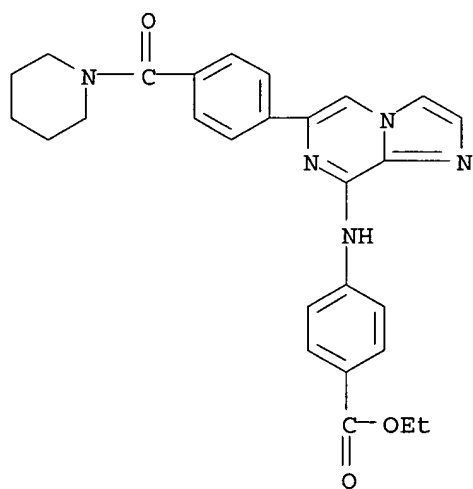
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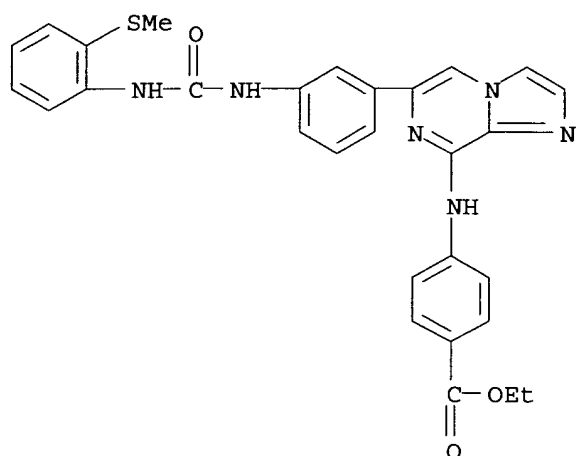
RN 618455-73-5 HCAPLUS

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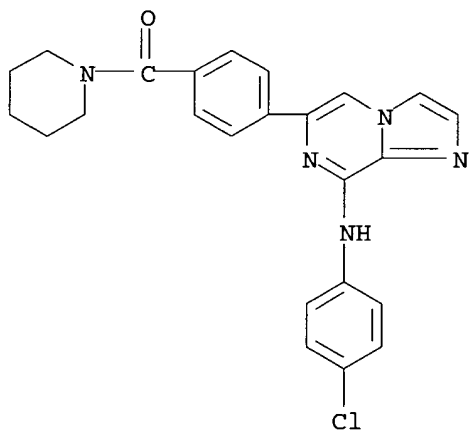
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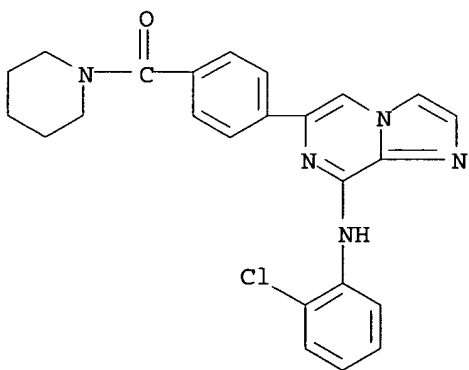
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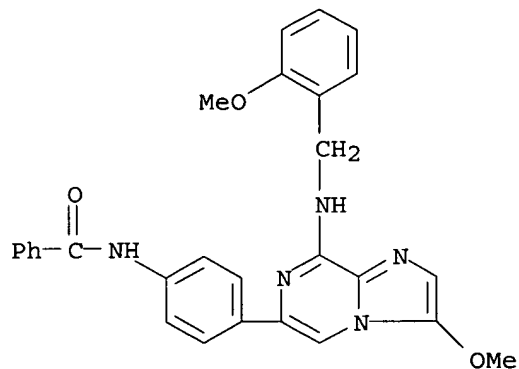


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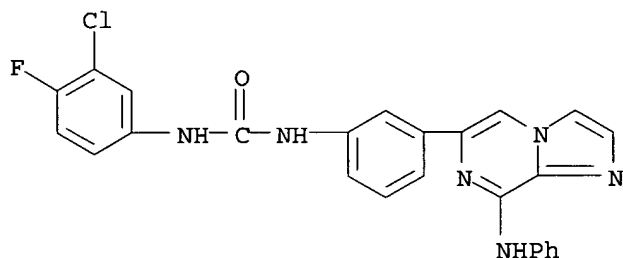
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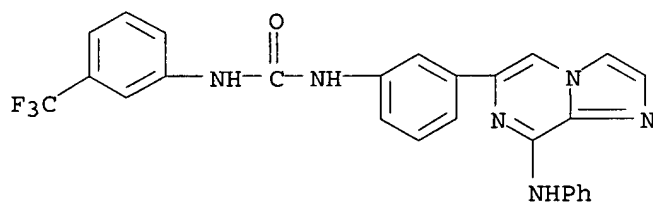
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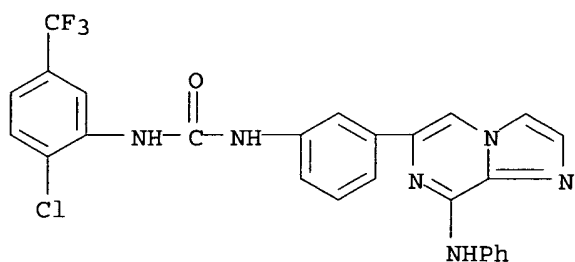
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RN 618455-86-0 HCAPLUS
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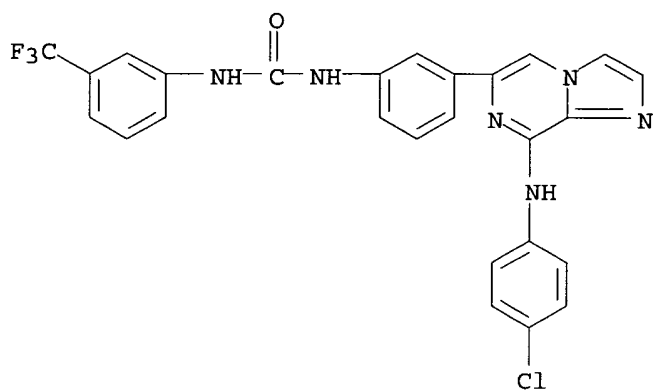


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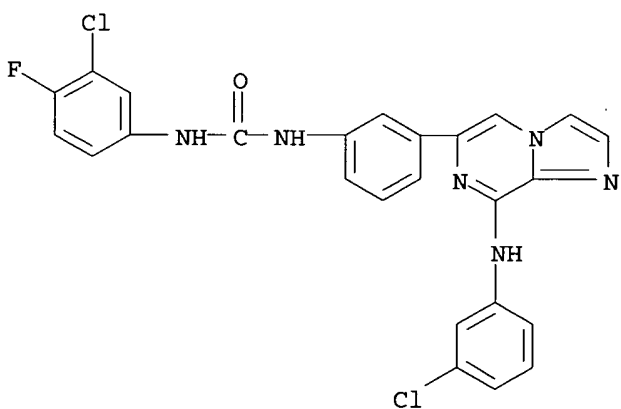
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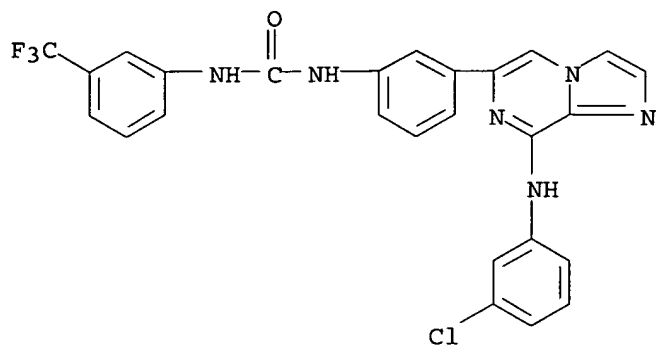
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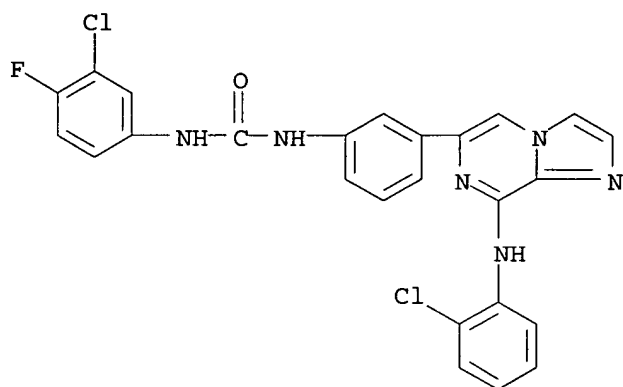


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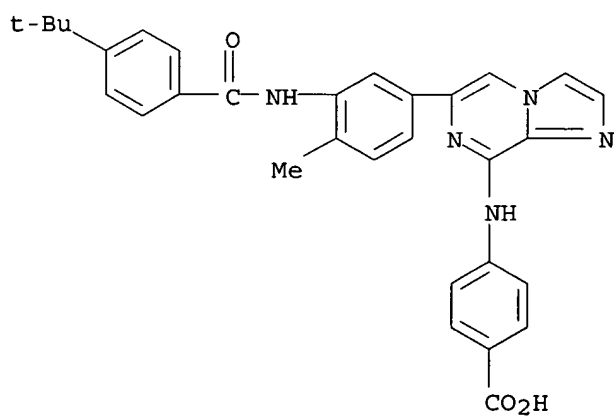
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RN 618455-99-5 HCAPLUS
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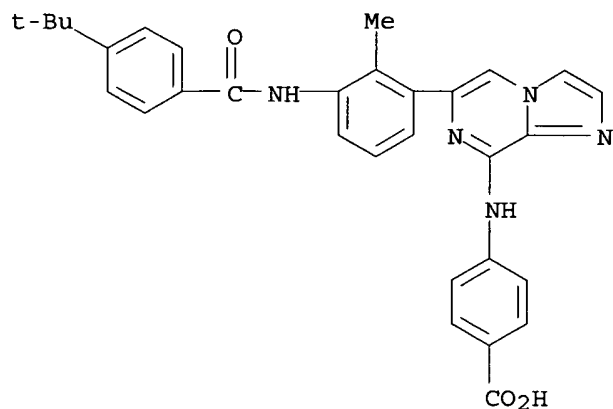


RN 852221-23-9 HCAPLUS
 CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]-4-methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



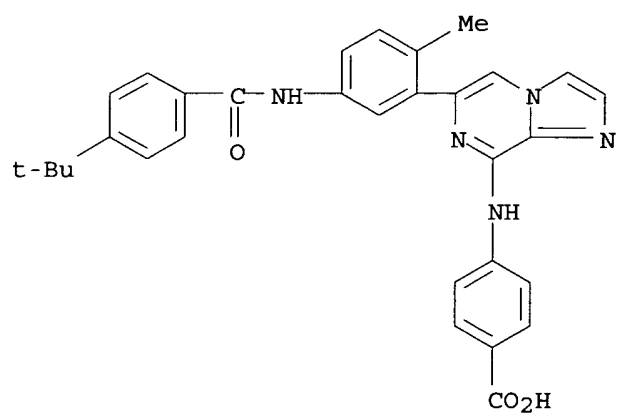
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methylphenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



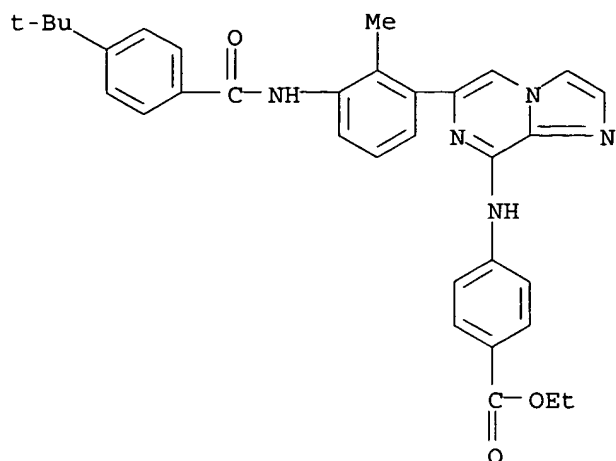
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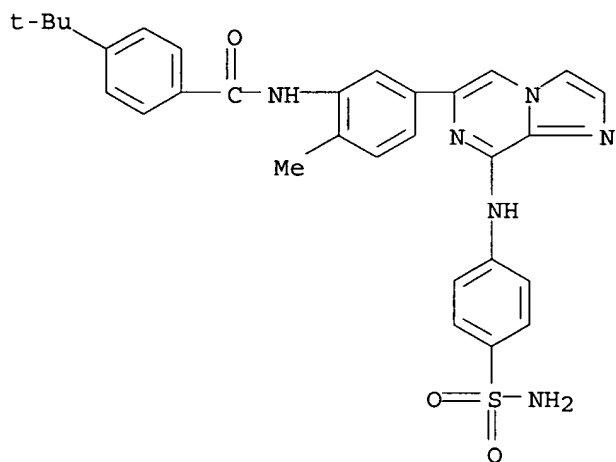
RN 852221-26-2 HCAPLUS

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RN 852221-27-3 HCAPLUS

CN Benzamide, N- [5- [8- [4- (aminosulfonyl)phenyl] amino] imidazo [1,2-a] pyrazin-6-yl] -2-methylphenyl] -4- (1,1-dimethylethyl) - (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:182665 HCAPLUS

DOCUMENT NUMBER: 142:280228

TITLE: Preparation of imidazo[1,2-a]pyrazines as modulators of protein kinases, particularly EphB4 kinase

INVENTOR(S): Mitchell, Scott A.; Desimone, Robert W.; Darrow, James W.; Pippin, Douglas A.; Danca, M. Diana

PATENT ASSIGNEE(S): Cellular Genomics Inc., USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

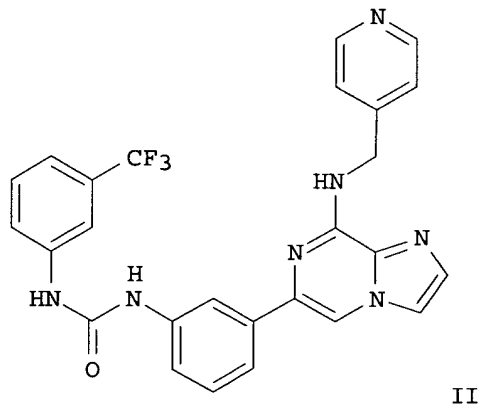
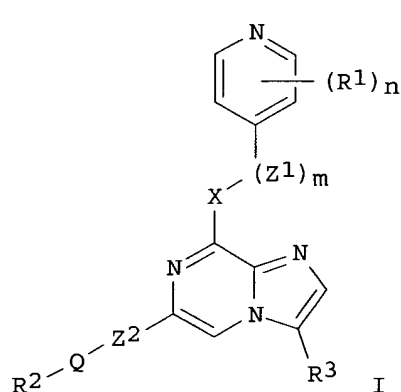
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

WO 2005019220 A2 20050303 WO 2004-US25884 20040811
 WO 2005019220 A3 20050324
 WO 2005019220 C2 20050602

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US 2005085484 A1 20050421 US 2004-915696 20040811
 PRIORITY APPLN. INFO.: US 2003-494179P P 20030811
 US 2004-540938P P 20040130
 US 2004-589738P P 20040721

OTHER SOURCE(S): MARPAT 142:280228
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AB Title compds. I [wherein n = 0-3; R₁ = hydroxy, nitro, cyano, amino or amido; R₃ = H or (un)substituted (cyclo)alkyl; m = 1-4; Z₁ = CR₄R₅; R₄, R₅ = H, alkyl or halo; Z₂ = Ph; Q = (un)substituted ureido; X = O, S, CH₂ or (un)substituted amino; R₂ = (un)substituted alkyl or aryl; etc., or pharmaceutically acceptable salts thereof] were prepared as kinase modulators, particularly, as inhibitors of angiogenic and oncogenic kinases. For instance, urea II was synthesized in 4 steps: (1) deprotection of BrCH₂CH(OMe)₂ with HBr and cyclocondensation with 3,5-dibromo-2-aminopyrazine to give 6,8-dibromoimidazo[1,2-a]pyrazine; (2) aminolysis of the 8-bromo with 4-aminomethylpyridine; (3) Suzuki coupling of the 6-bromo with 3-H₂NC₆H₄B(OH)₂; and (4) carbamoylation of the amino group with 3-trifluoromethylphenyl isocyanate. In an assay for EphB4 kinase activity, using human recombinant EphB4 kinase cytoplasmic domain, compds. I had IC₅₀ values of 1 μM or less, with some particularly preferred compds. having values of 100 nM or less. Similar inhibitory potencies were found against PDGF-Rα, VEGF-R2, c-Kit, and Tie-2 kinases in vitro. Therefore, I and pharmaceutical compns. are useful for treating diseases and disorders responsive to modulation of at least one

of EphB4, PDGF-R α , VEGF-R2, c-Kit, and Tie-2 kinases, such as cancer.

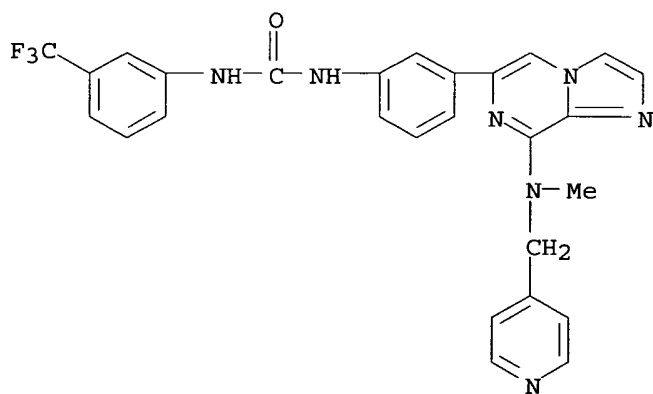
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(inhibitor; preparation of imidazopyrazines as kinase inhibitors)

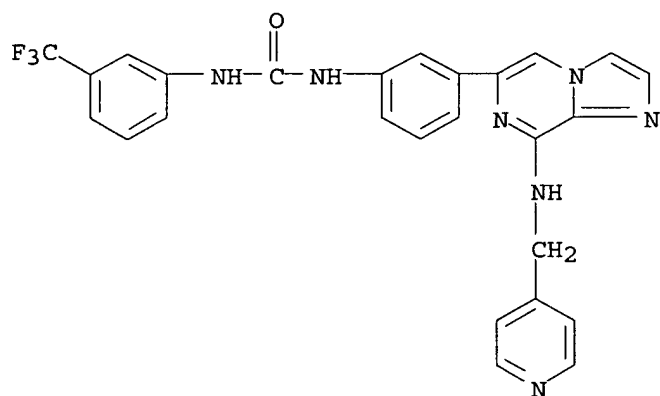
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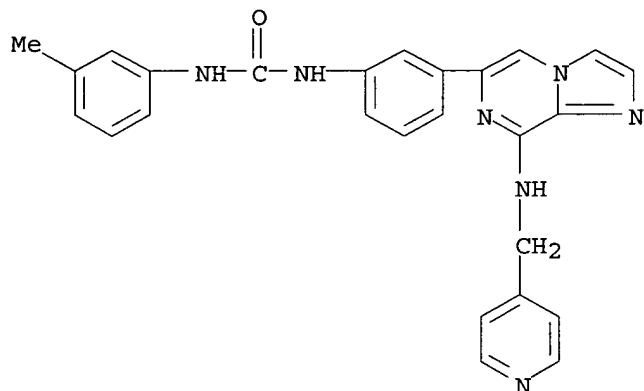
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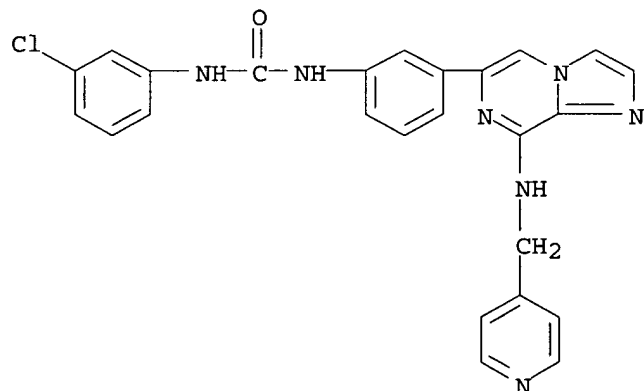
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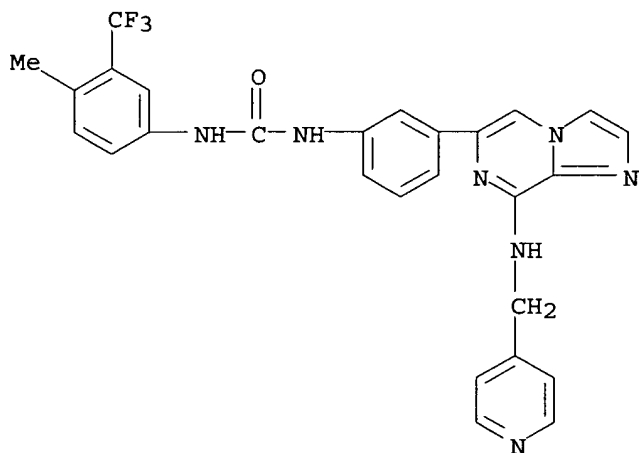
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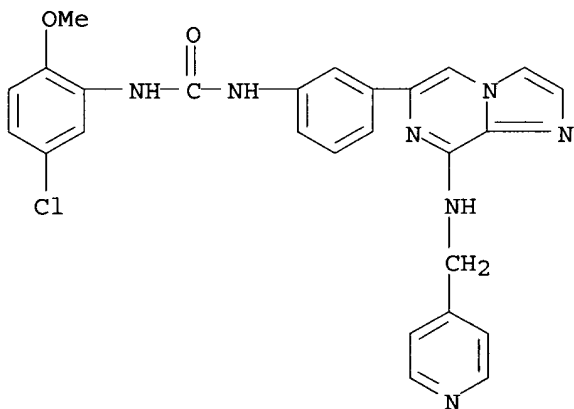


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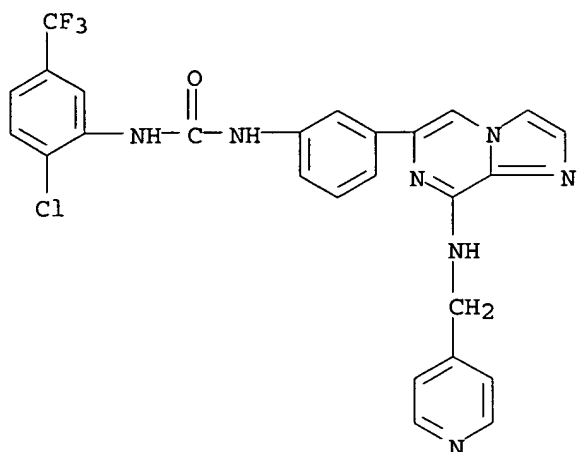
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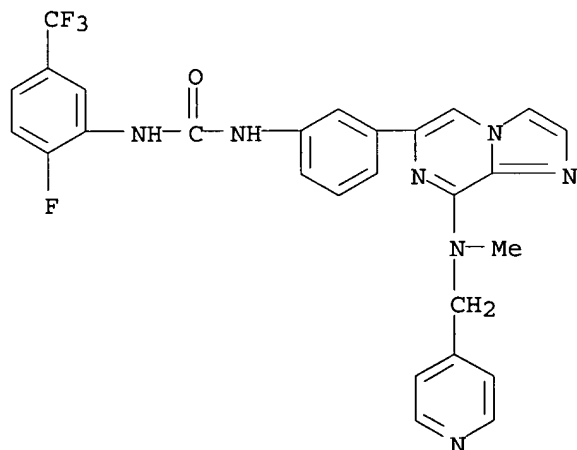
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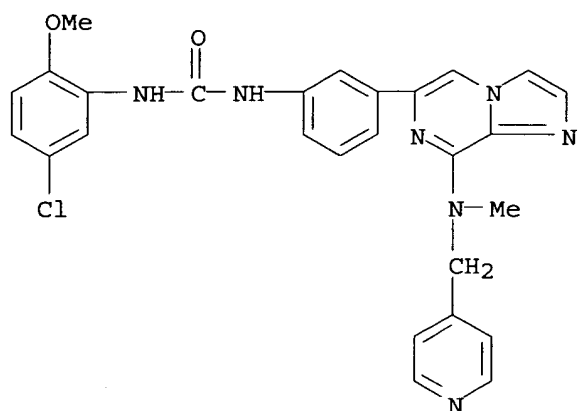
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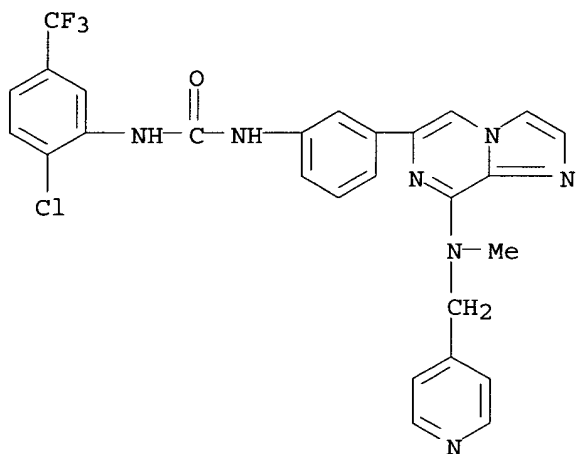


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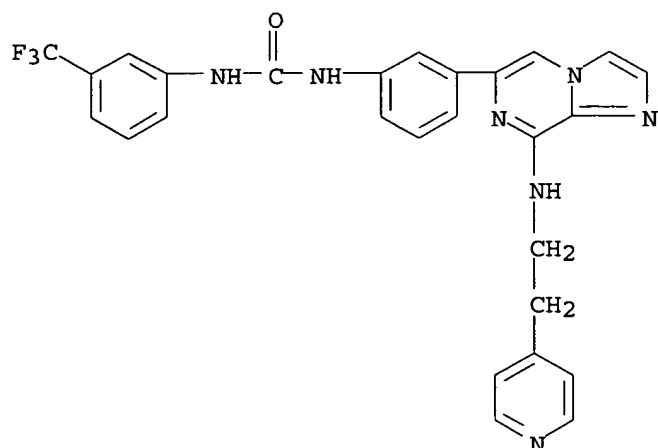
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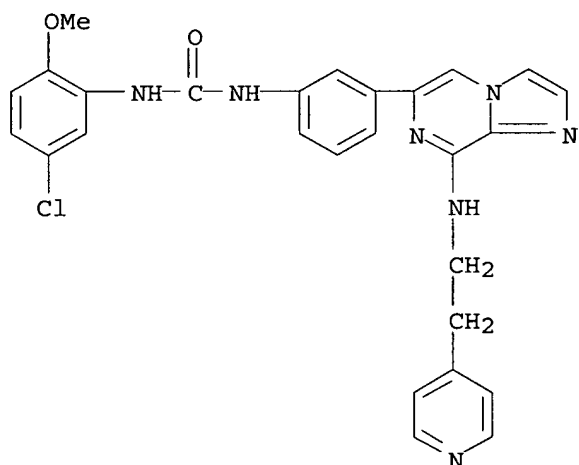


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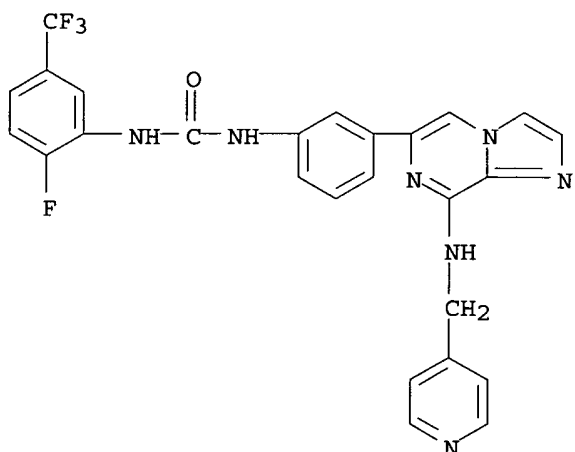
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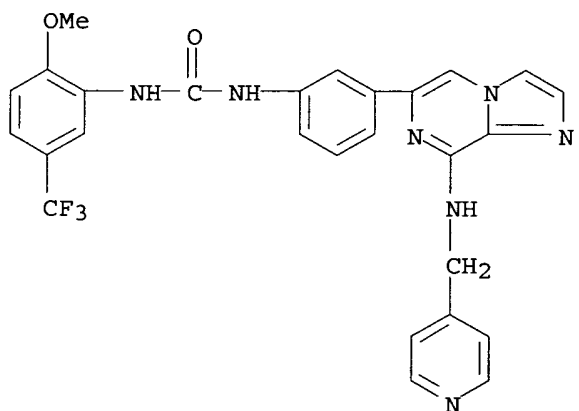


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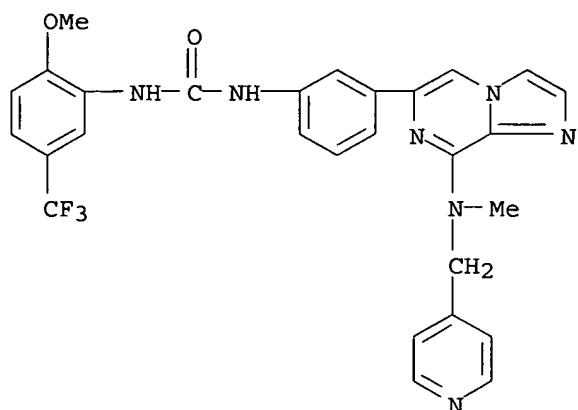
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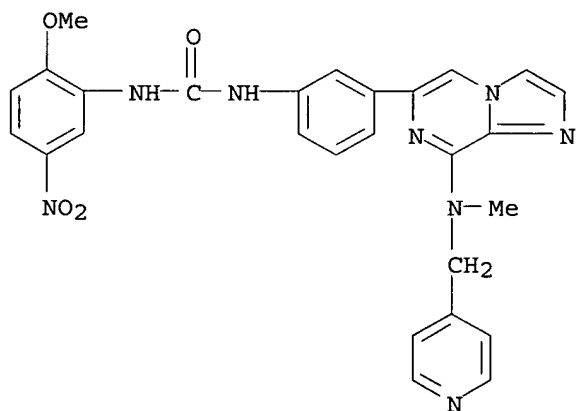


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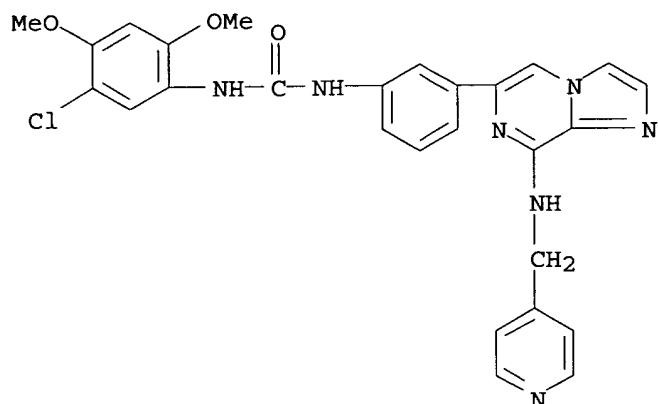
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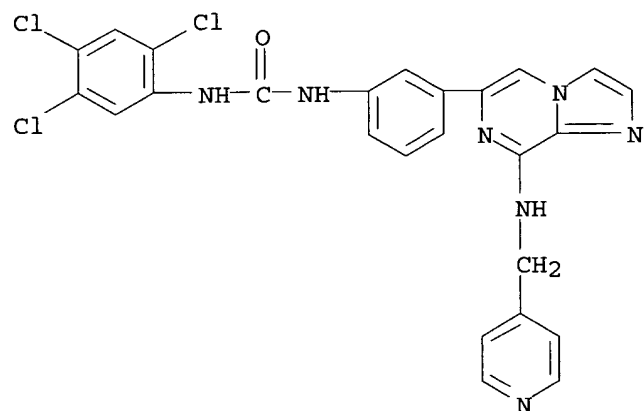


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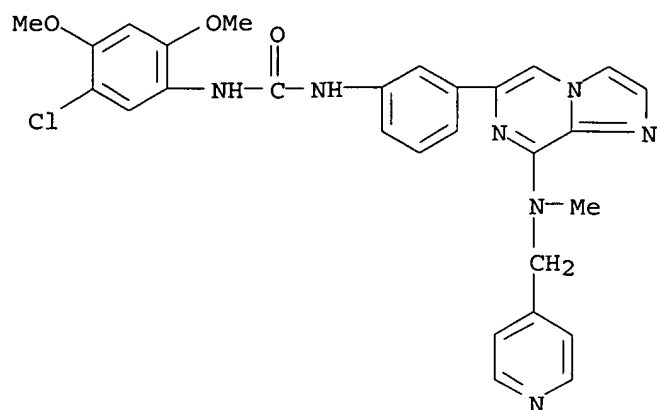
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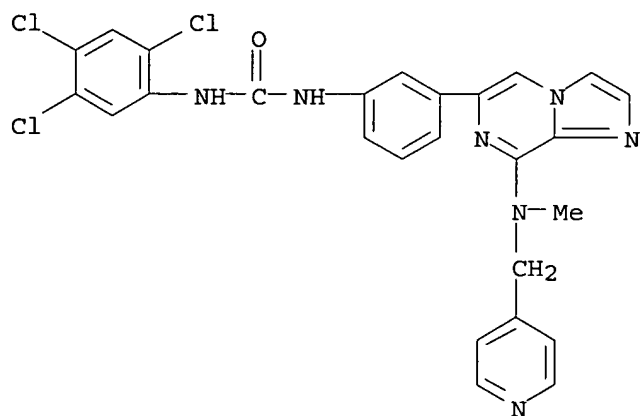
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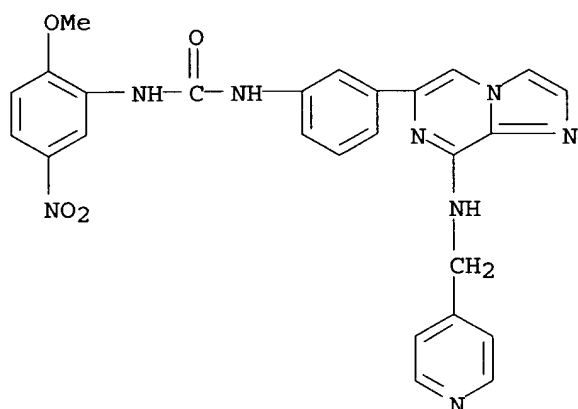
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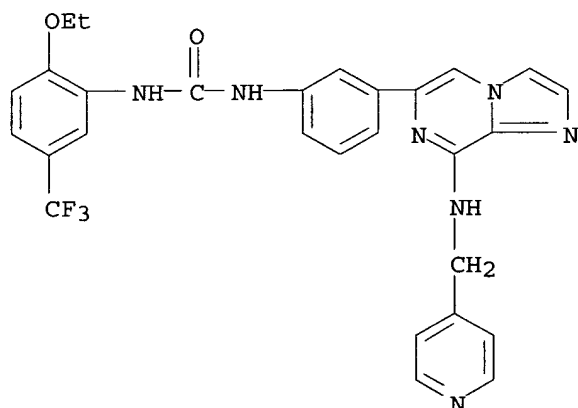
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CN Urea, N-(2-methoxy-5-nitrophenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



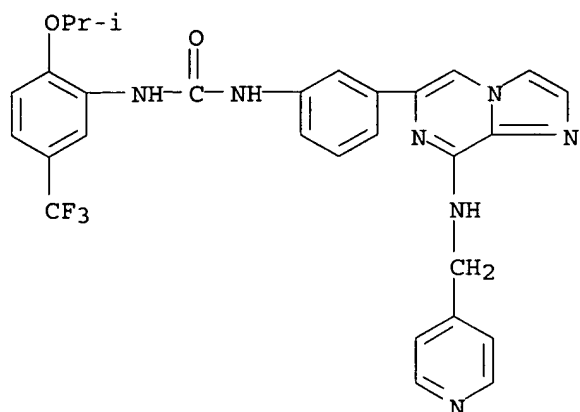
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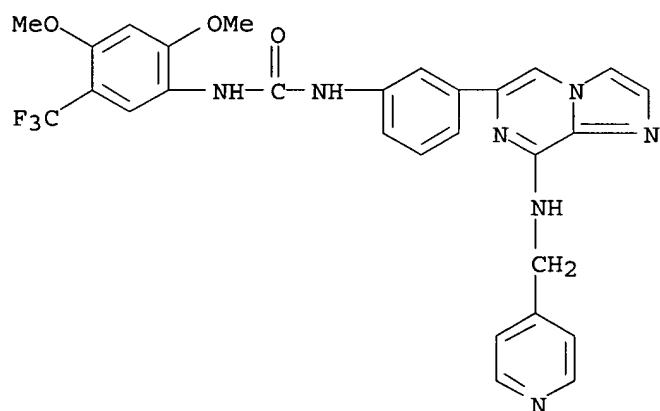
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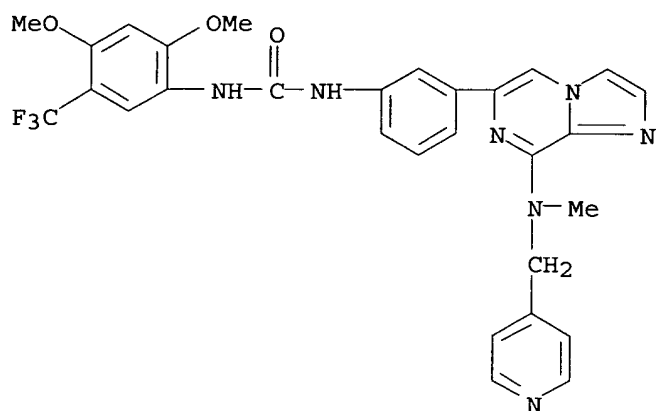
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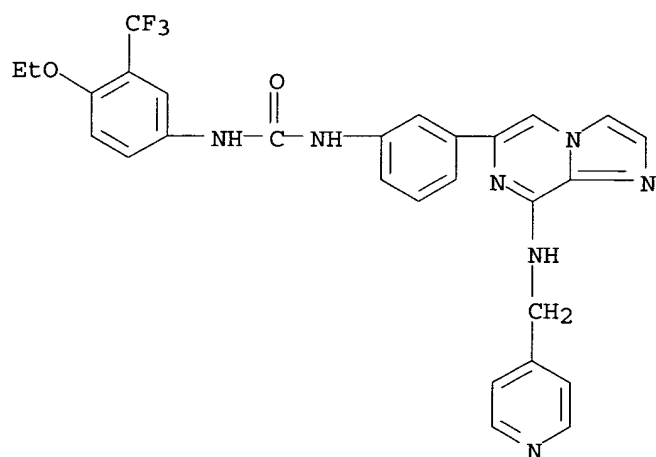
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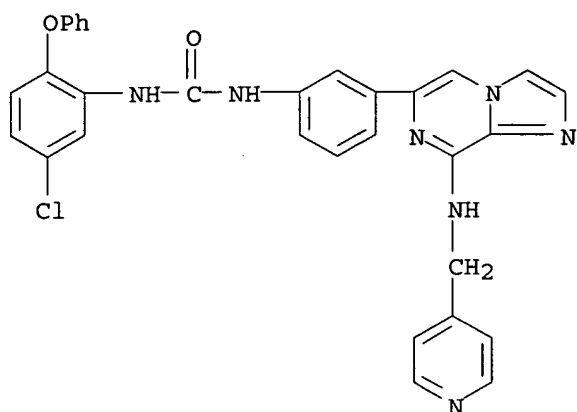
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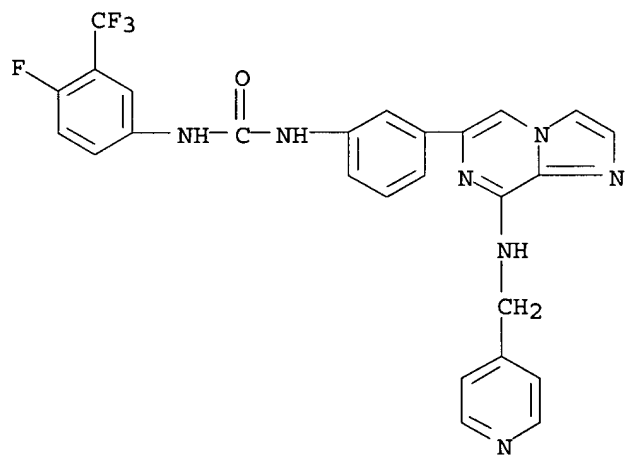
RN 847024-49-1 HCAPLUS

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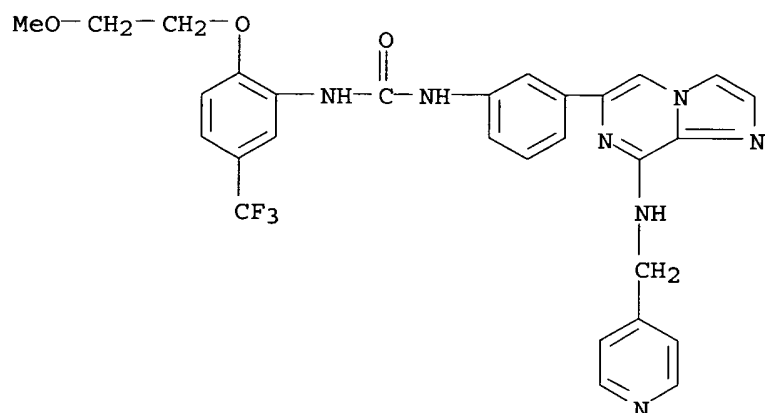
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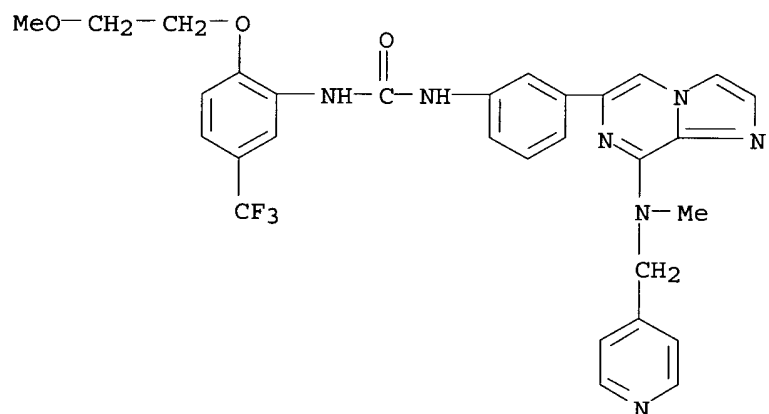
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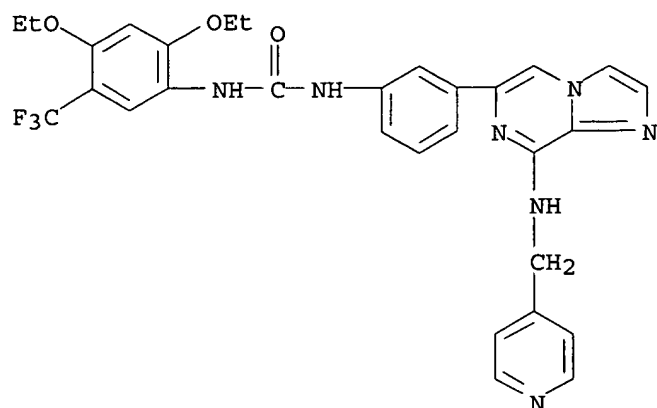
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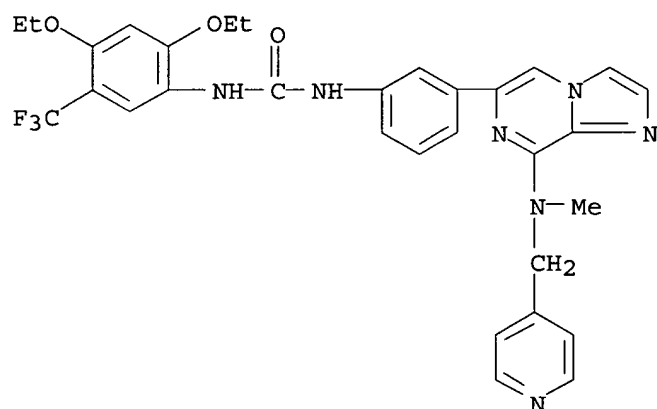
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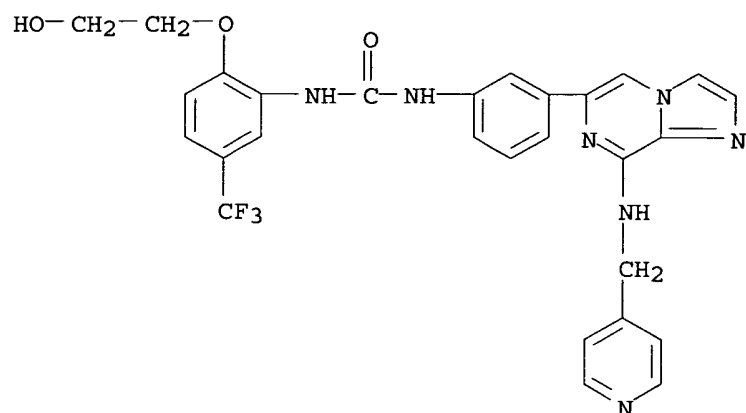
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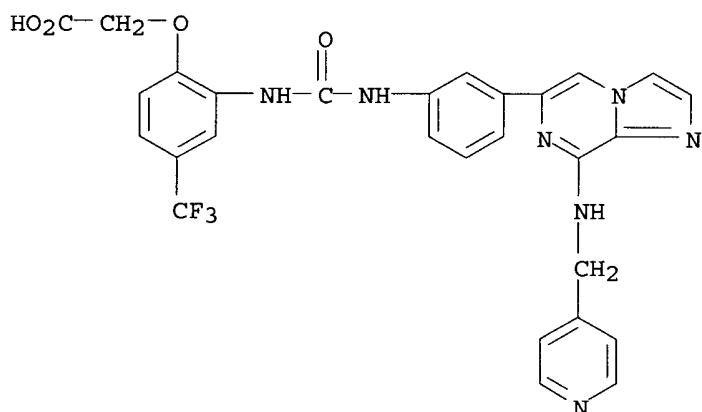
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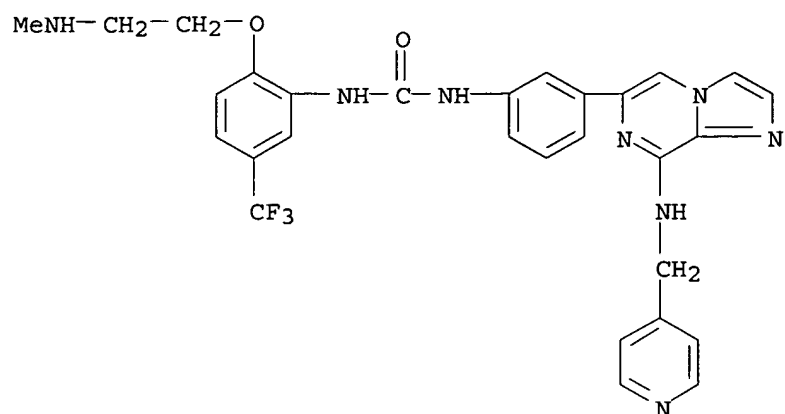
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CN Acetic acid, [2-[[[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]amino]-4-(trifluoromethyl)phenoxy]-(9CI) (CA INDEX NAME)



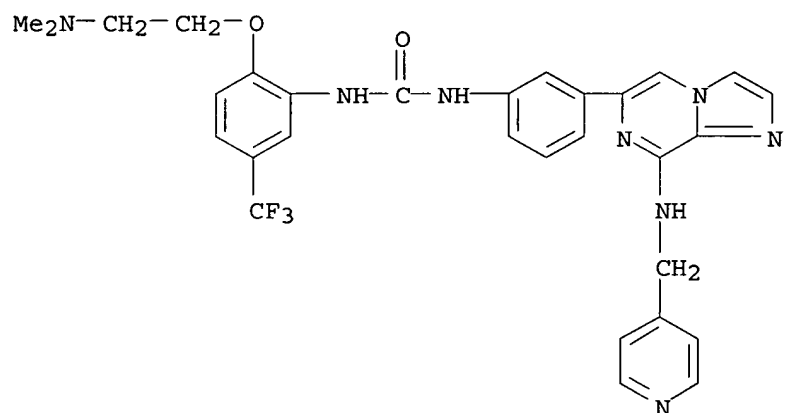
RN 847024-57-1 HCAPLUS

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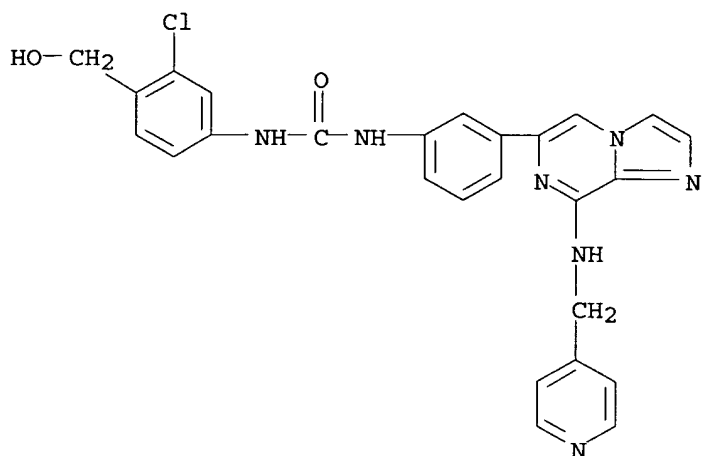
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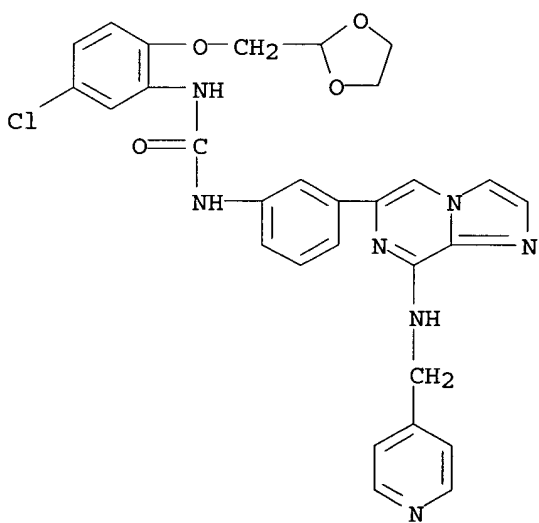
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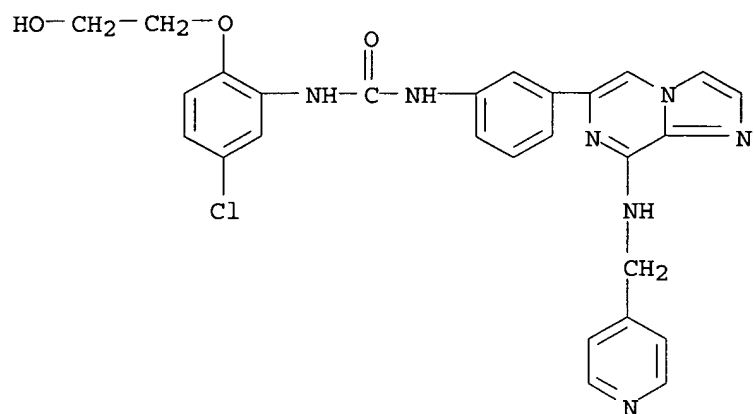
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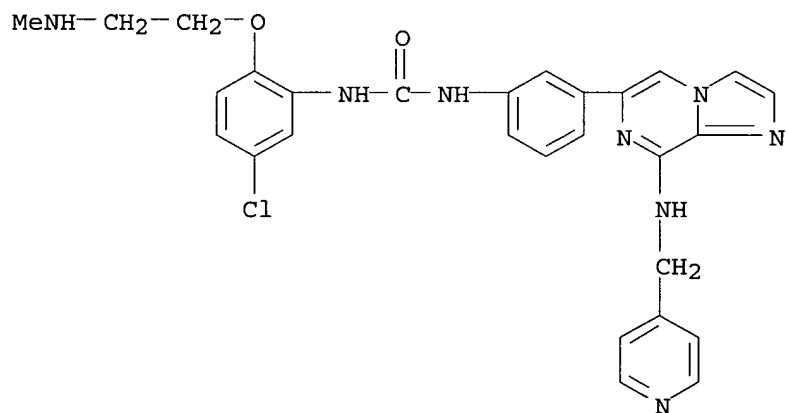
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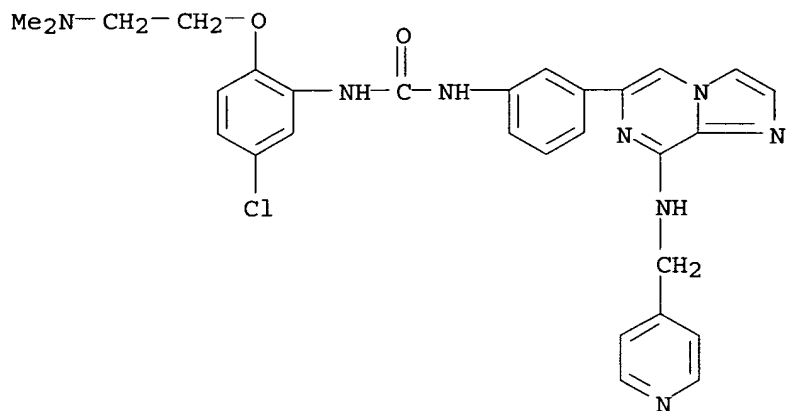
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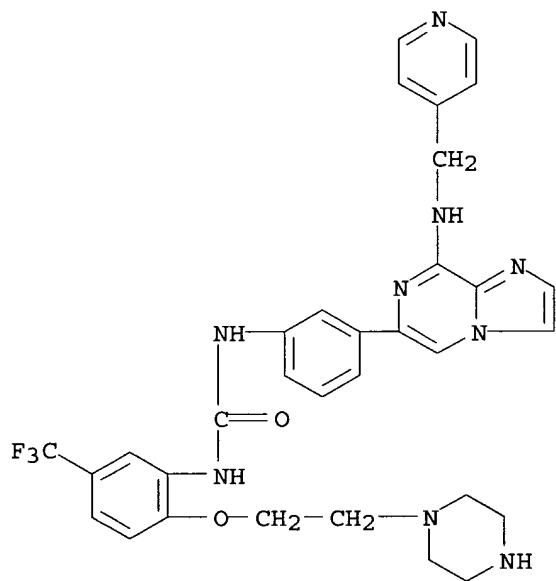


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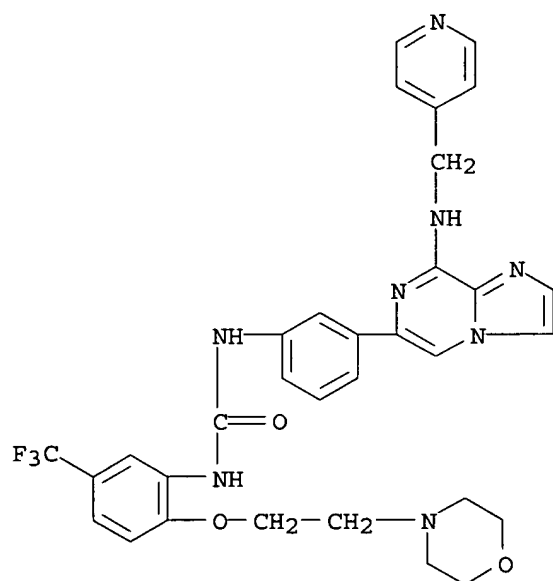
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RN 847024-64-0 HCAPLUS
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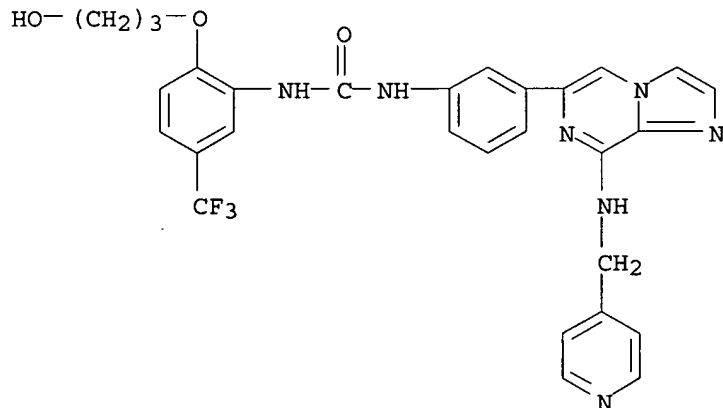


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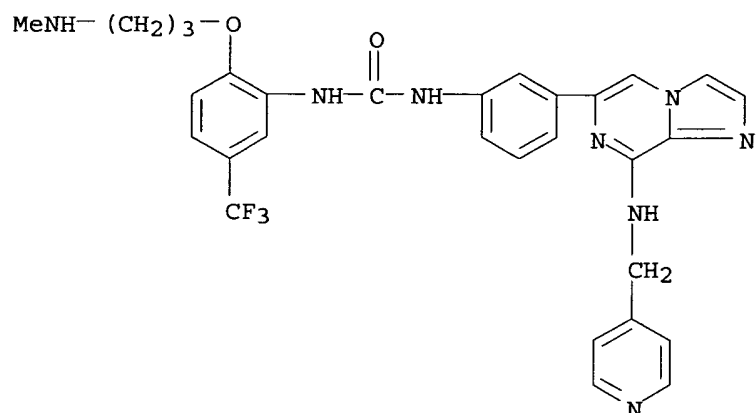
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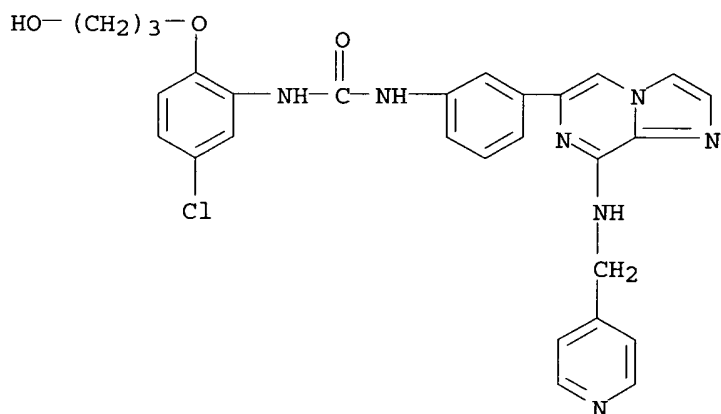
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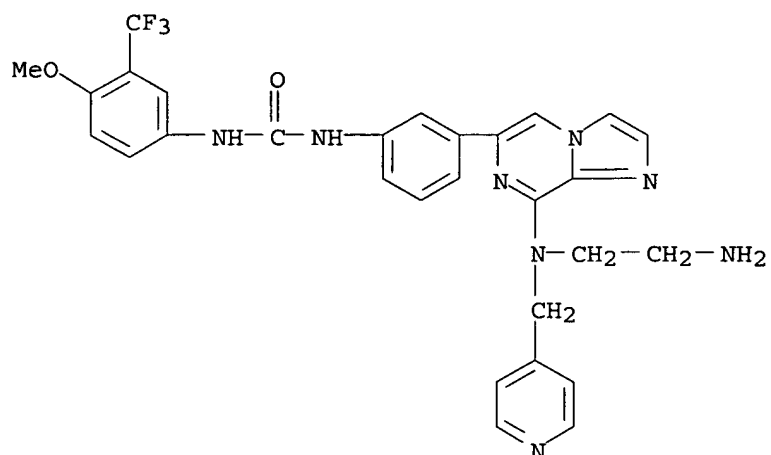
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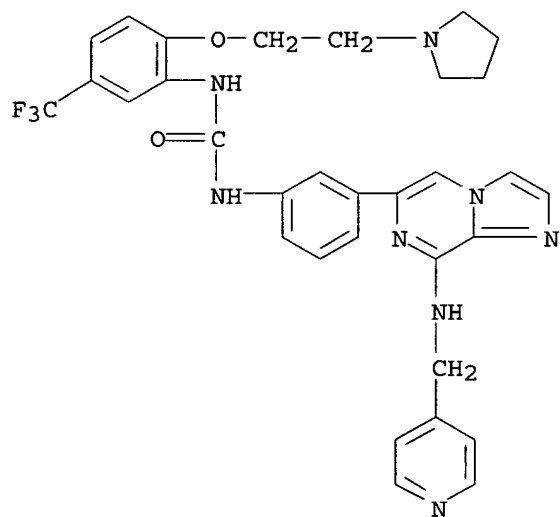
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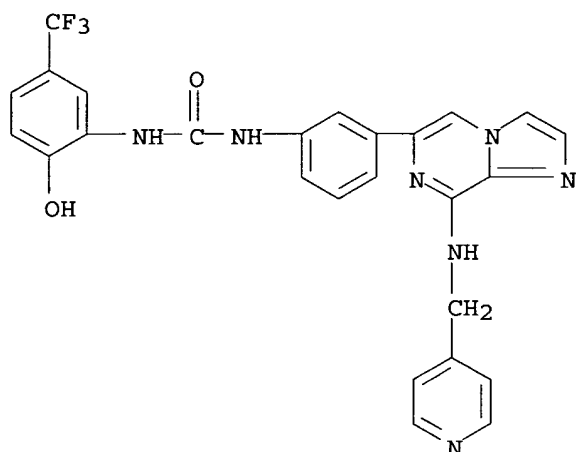
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RN 847024-71-9 HCAPLUS

CN Urea, N-[2-hydroxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



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ACCESSION NUMBER: 2005:141072 HCAPLUS

DOCUMENT NUMBER: 142:240469

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines for inhibition of bruton's tyrosine kinase

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Mitchell, Scott A.; Pippin, Douglas A.; Darrow, James W.; Qian, Xiaobing; Velleca, Mark; Qian, Dapeng

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 181 pp.

CODEN: PIXXD2

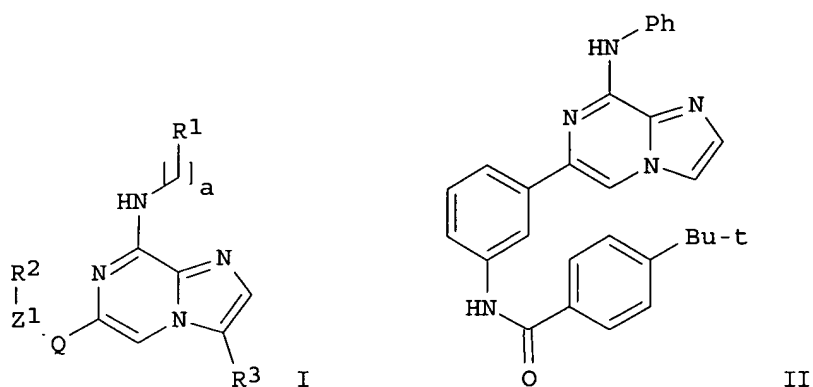
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2005014599 | A1 | 20050217 | WO 2004-US18227 | 20040604 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2005090499 | A1 | 20050428 | US 2004-861791 | 20040604 |
| PRIORITY APPLN. INFO.: | | | US 2003-475634P | P 20030604 |
| | | | US 2003-519311P | P 20031111 |
| OTHER SOURCE(S): | MARPAT 142:240469 | | | |
| GI | | | | |



AB The title compds. I [a = 0-1; R¹ = substituted Ph, heteroaryl; R² = alkyl, alkoxyalkoxy, (heterocycloalkyl)alkyl, (cycloalkyl)alkyl, etc.; Z¹ = CONR⁴, NR⁴CO; R⁴ = H, alkyl, cycloalkyl, etc.; Q = Ph, pyridyl; R³ = H, halo, alkyl, etc.], useful for treating diseases responsive to inhibition of Btk activity and/or B-cell proliferation such as cancer, an autoimmune and/or inflammatory disease, or an acute inflammatory reaction, were prepared E.g., a multi-step synthesis of II (no characterization data for intermediates), starting from 3,5-dibromo-2-aminopyrazine, was given. The exemplified compds. I were tested in the Btk biochem. assay and found to exhibit an IC₅₀ value less than or equal to 1 μM. Pharmaceutical compns. containing one or more compds. I, or a pharmaceutically acceptable form of such compds., and one or more pharmaceutically acceptable carriers, excipients, or diluents are provided herein. Other embodiments include methods of treating human and animals, including livestock and domesticated companion animals, suffering from a disease responsive to inhibition of Btk activity. Methods of treatment include administering a compound I as a single active agent or administering a compound I in combination with one or more other therapeutic agent. A method for determining the presence of Btk in a sample, comprising contacting the sample with a compound I under conditions that permit detection of Btk activity, detecting a level of Btk activity in the sample, and therefrom determining the presence

or

absence of Btk in the sample, is also disclosed.

IT 845269-72-9P 845269-73-0P 845269-74-1P
 845269-75-2P 845269-76-3P 845269-77-4P
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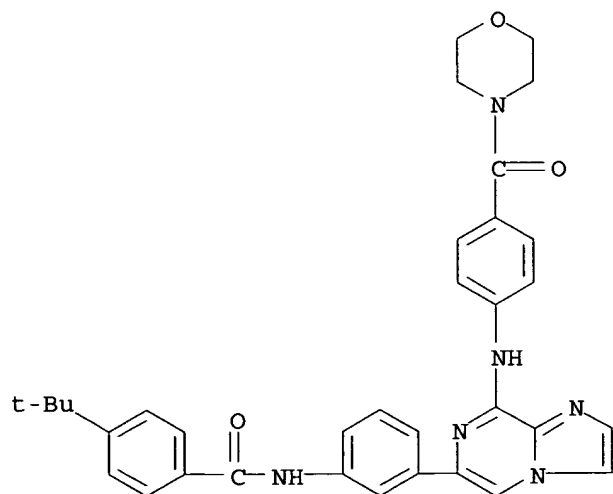
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of imidazo[1,2-a]pyrazin-8-ylamines for inhibition of bruton's tyrosine kinase)

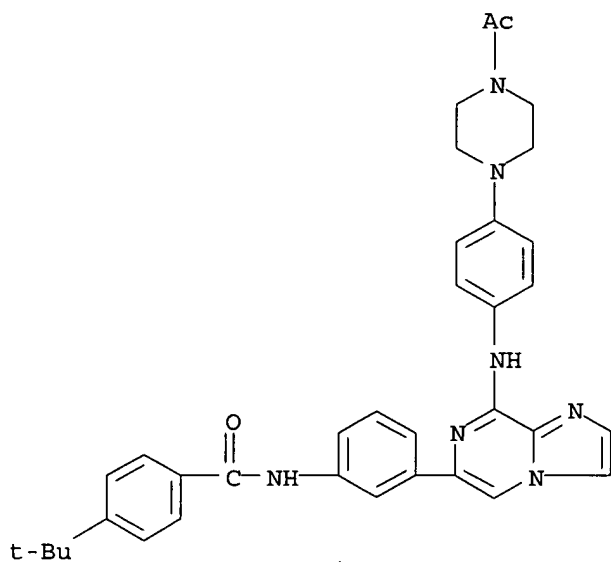
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CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
 (CA INDEX NAME)



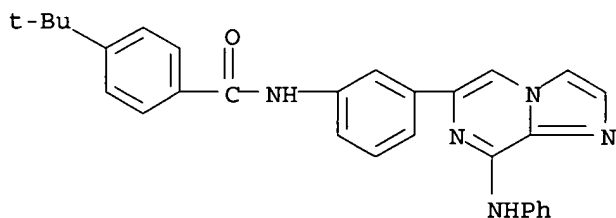
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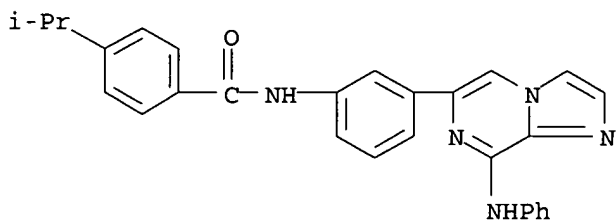
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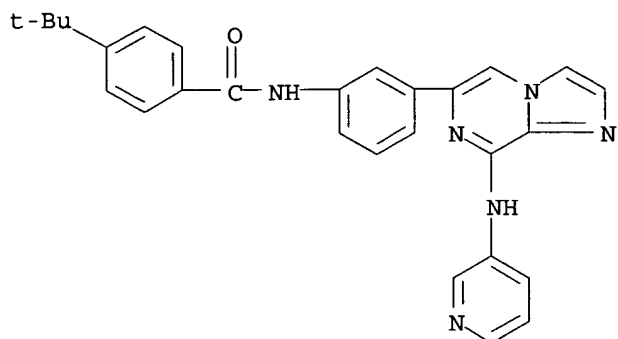
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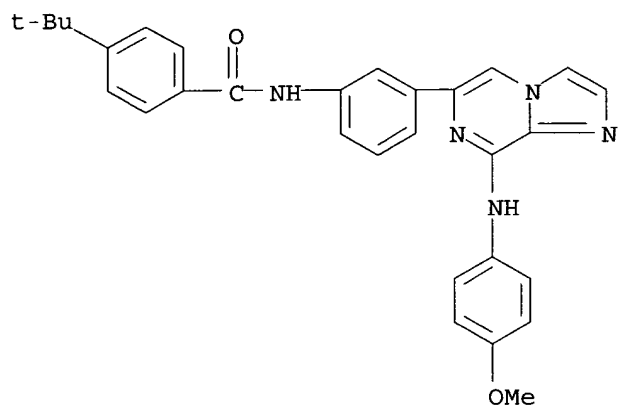
RN 845269-76-3 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-(3-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



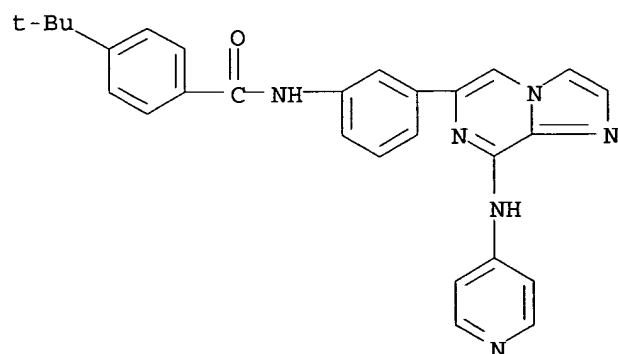
RN 845269-77-4 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(4-methoxyphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



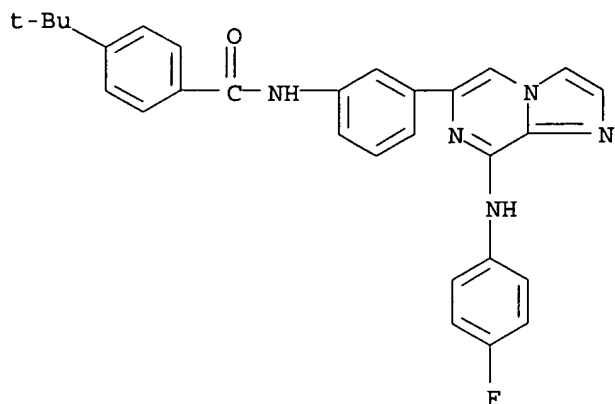
RN 845269-78-5 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-(4-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

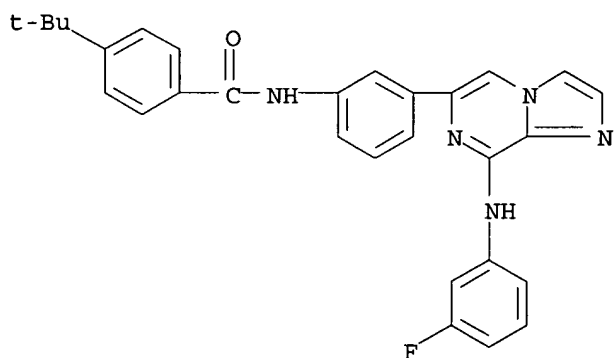


RN 845269-79-6 HCAPLUS

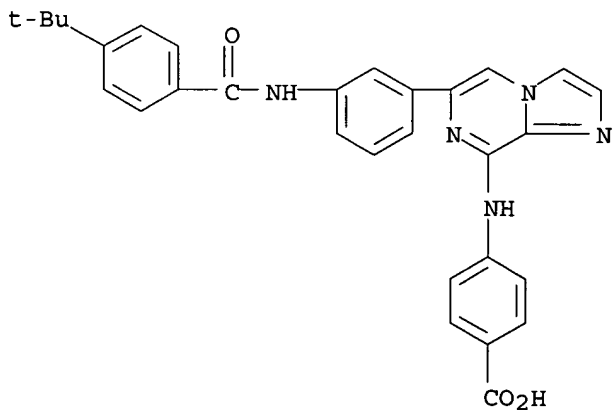
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(4-fluorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845269-80-9 HCAPLUS
 CN Benamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(3-fluorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

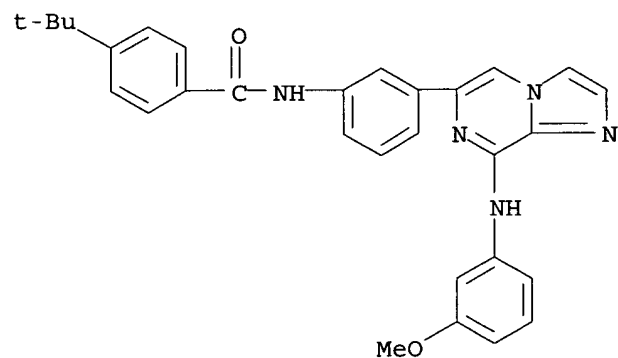


RN 845269-81-0 HCAPLUS
 CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



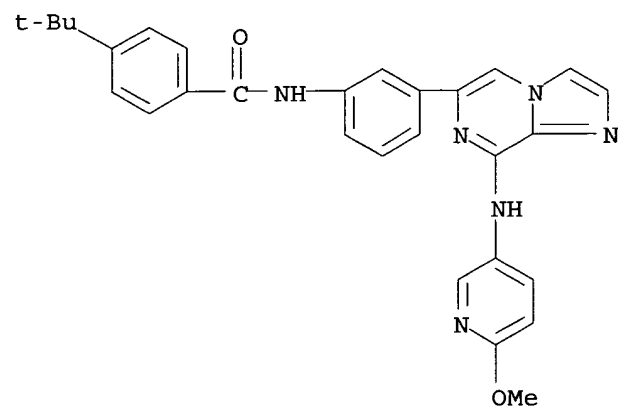
RN 845269-82-1 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(3-methoxyphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



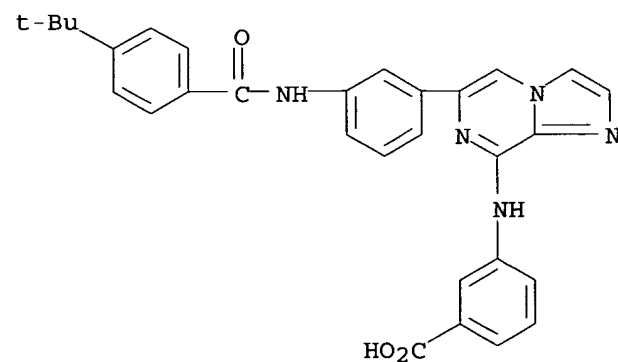
RN 845269-83-2 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(6-methoxy-3-pyridinyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

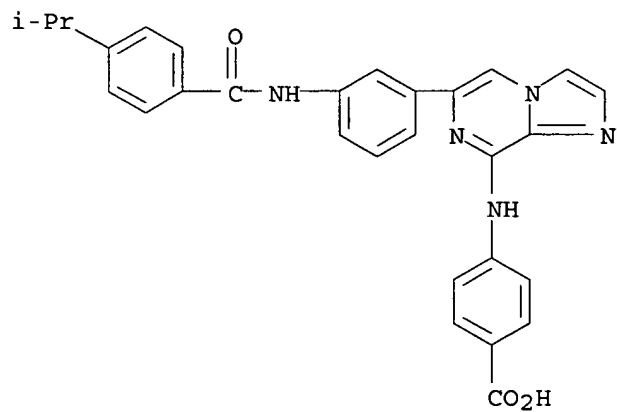


RN 845269-84-3 HCAPLUS

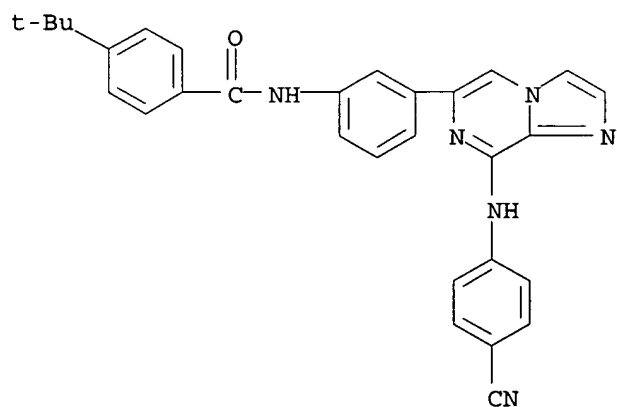
CN Benzoic acid, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



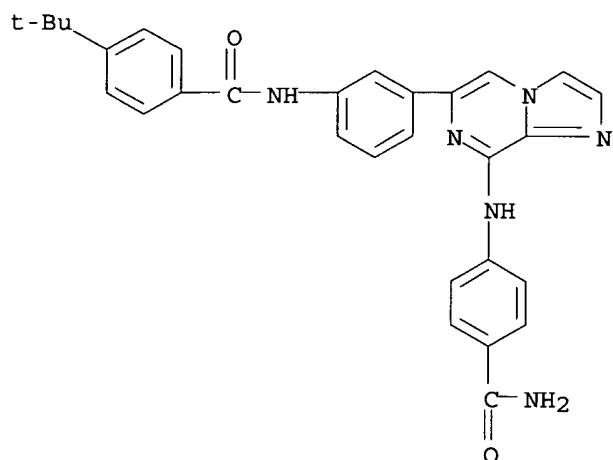
RN 845269-85-4 HCAPLUS
 CN Benzoic acid, 4-[[6-[3-[[4-(1-methylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



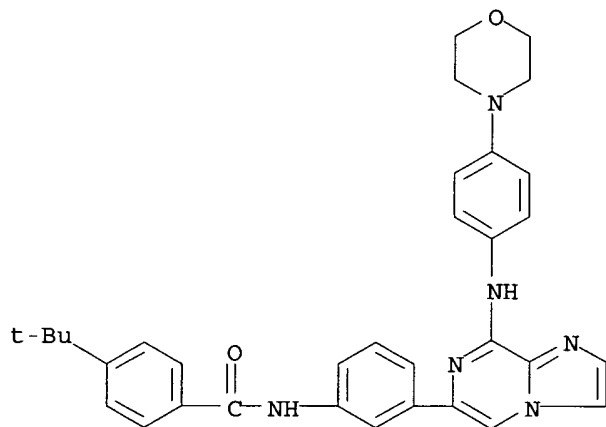
RN 845269-86-5 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-cyanophenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



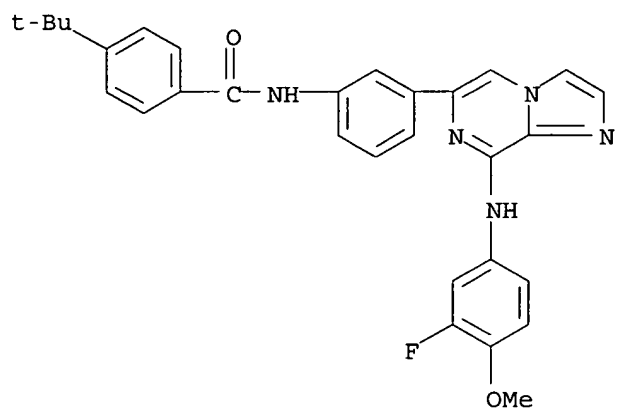
RN 845269-87-6 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-(aminocarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 845269-88-7 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-aminocarbonylphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)

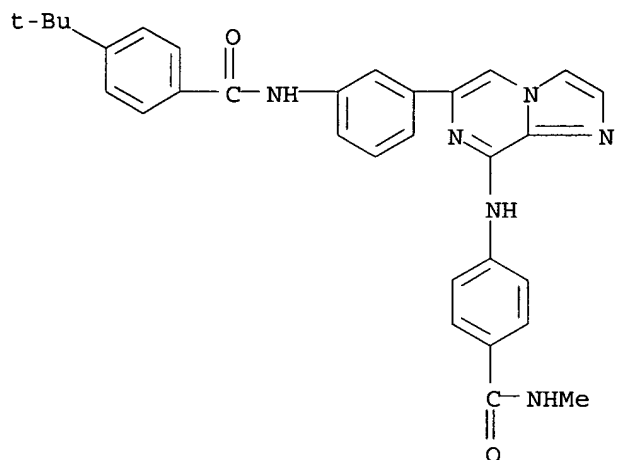


RN 845269-89-8 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-fluoro-4-methoxyphenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



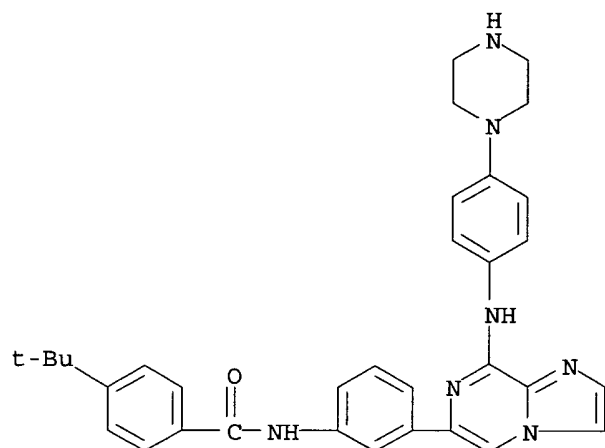
RN 845269-90-1 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl-2-fluorophenyl]benzamide (9CI) (CA INDEX NAME)



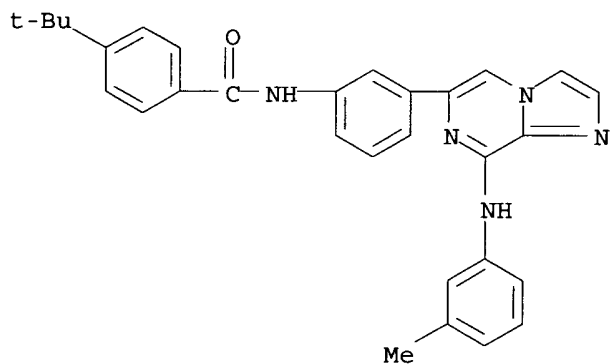
RN 845269-91-2 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



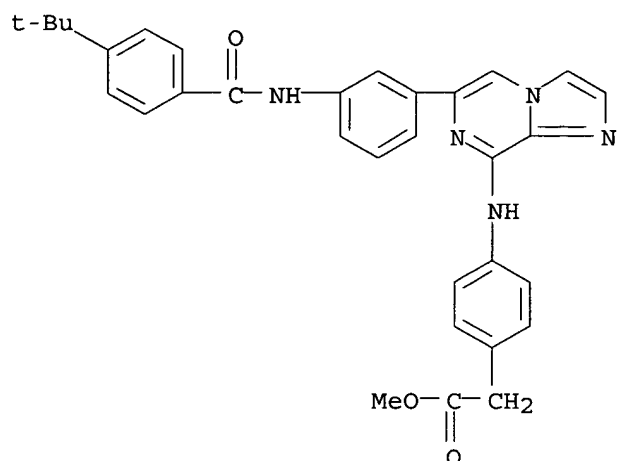
RN 845269-92-3 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(3-methylphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



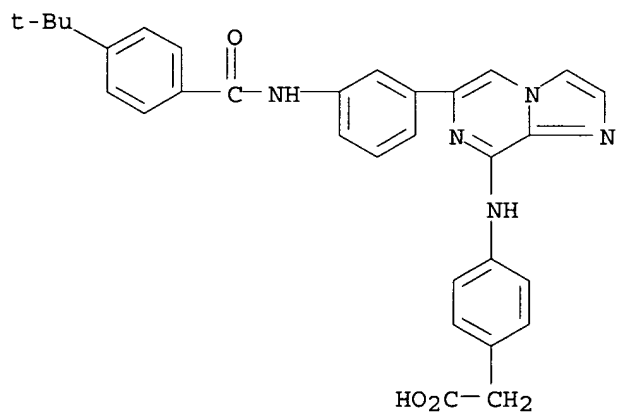
RN 845269-93-4 HCAPLUS

CN Benzeneacetic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)



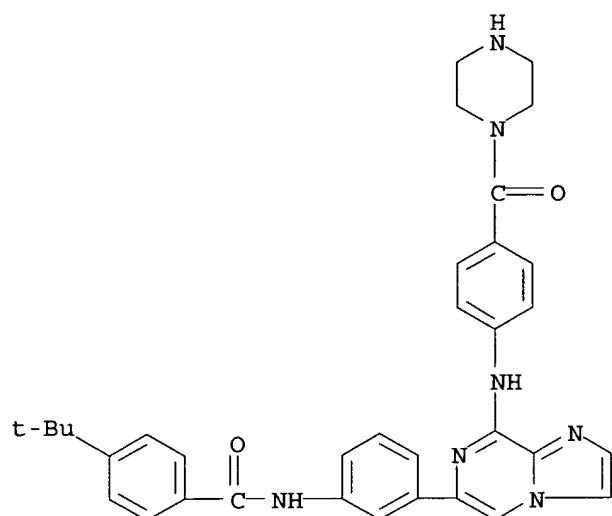
RN 845269-94-5 HCAPLUS

CN Benzeneacetic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



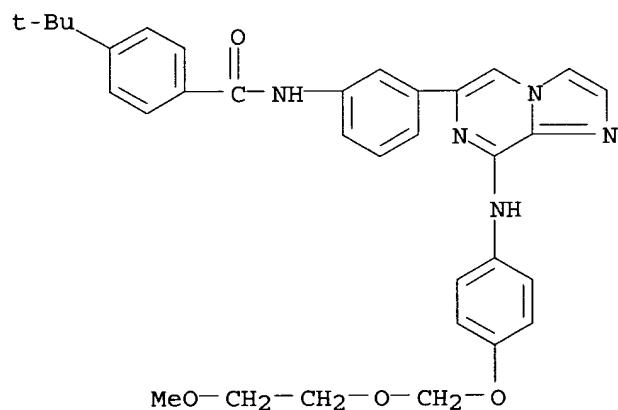
RN 845269-95-6 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



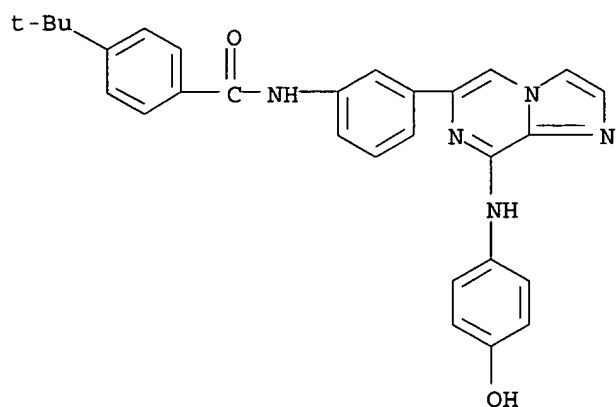
RN 845269-96-7 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(2-methoxyethoxy)methoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)

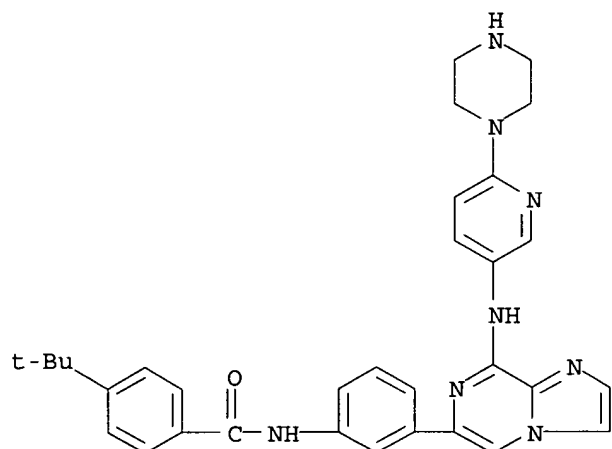


RN 845269-97-8 HCAPLUS

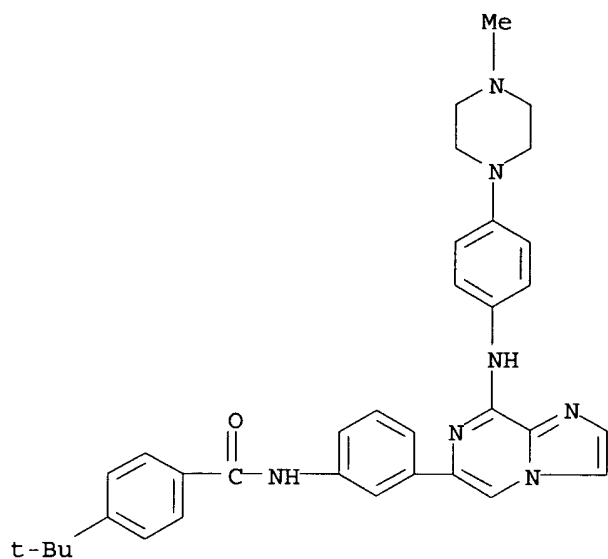
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[(4-hydroxyphenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



RN 845269-98-9 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[6-(1-piperazinyl)-3-pyridinyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

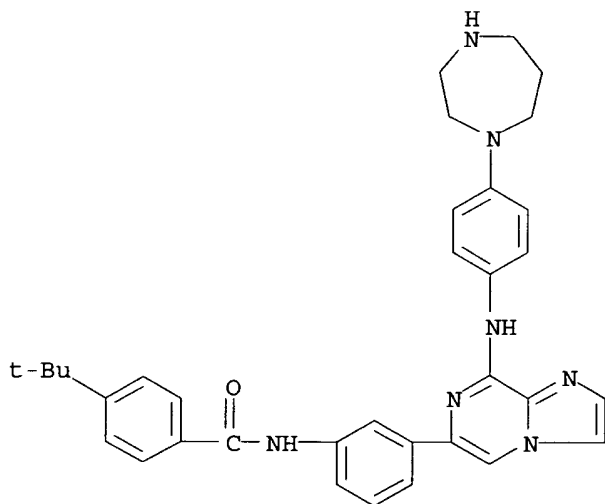


RN 845269-99-0 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-methyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



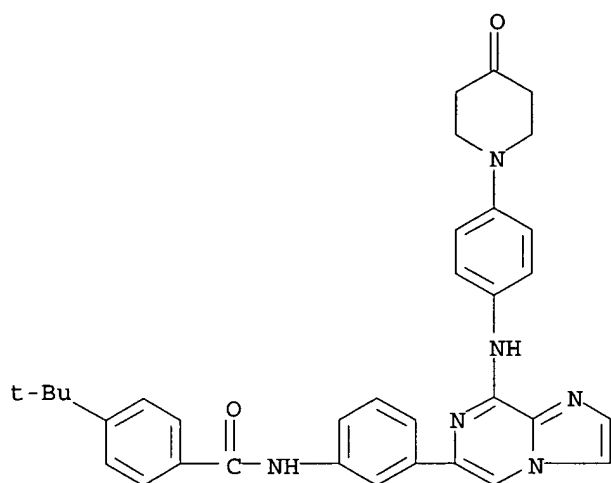
RN 845270-00-0 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(hexahydro-1H-1,4-diazepin-1-yl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



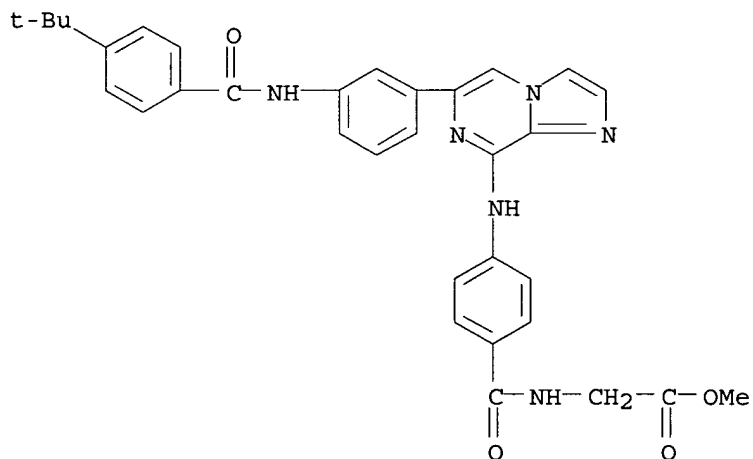
RN 845270-01-1 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-oxo-1-piperidinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



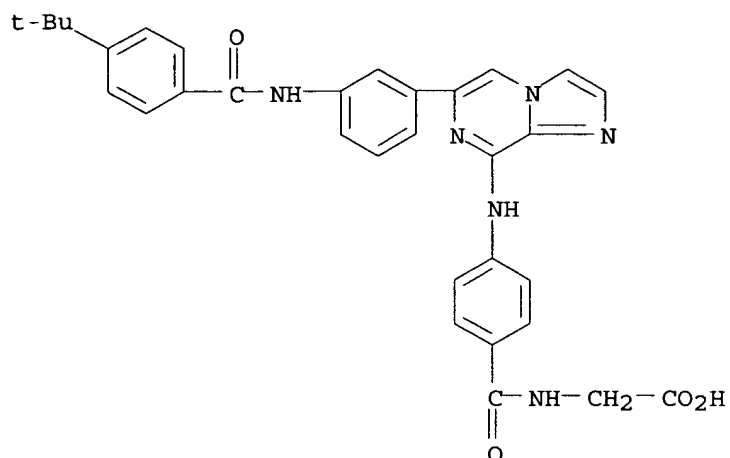
RN 845270-02-2 HCAPLUS

CN Glycine, N-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]-, methyl ester (9CI) (CA INDEX NAME)

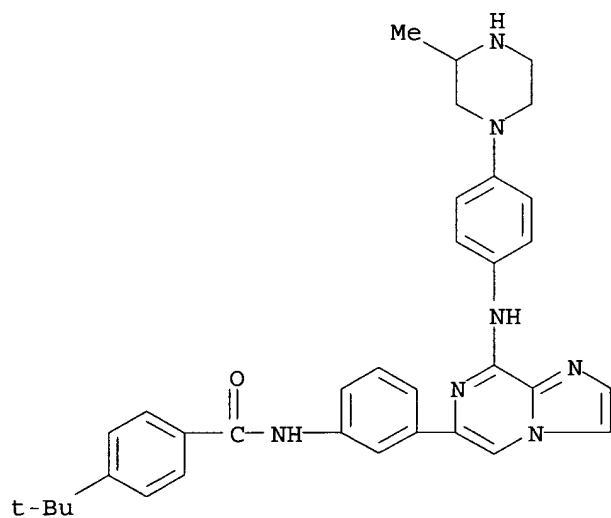


RN 845270-03-3 HCAPLUS

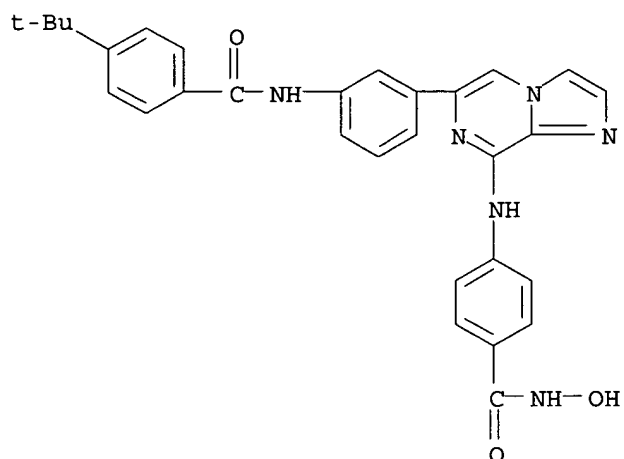
CN Glycine, N-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoyl]- (9CI) (CA INDEX NAME)



RN 845270-04-4 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[4-(3-methyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

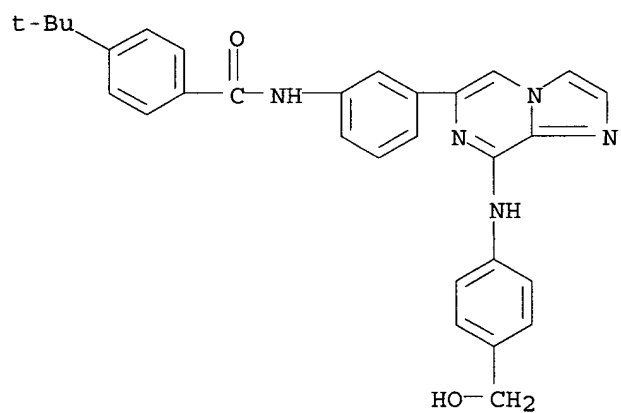


RN 845270-05-5 HCAPLUS
 CN Benzamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-hydroxy- (9CI) (CA INDEX NAME)



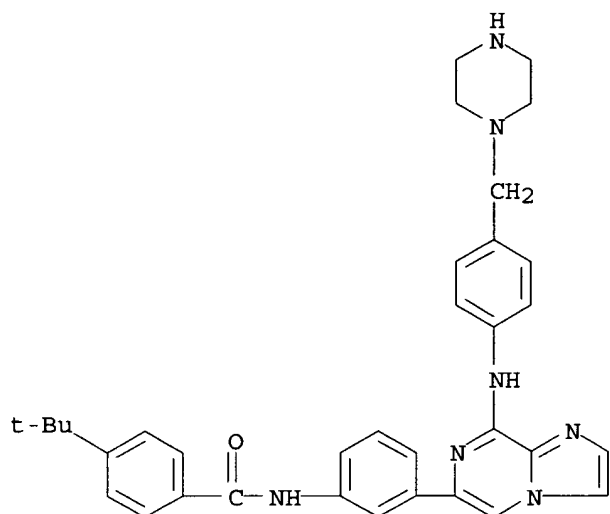
RN 845270-06-6 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(hydroxymethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



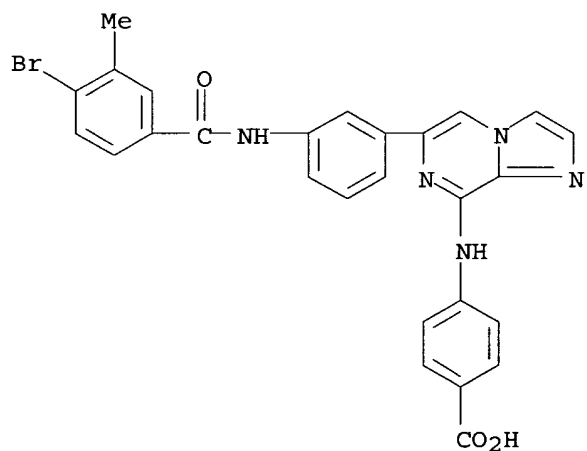
RN 845270-07-7 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-piperazinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



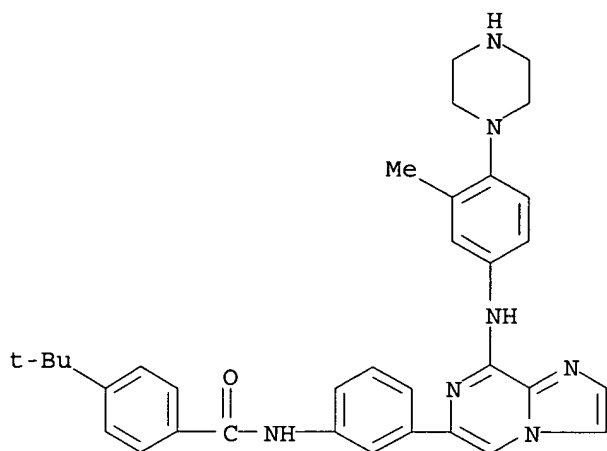
RN 845270-08-8 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[(4-bromo-3-methylbenzoyl)amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



RN 845270-09-9 HCAPLUS

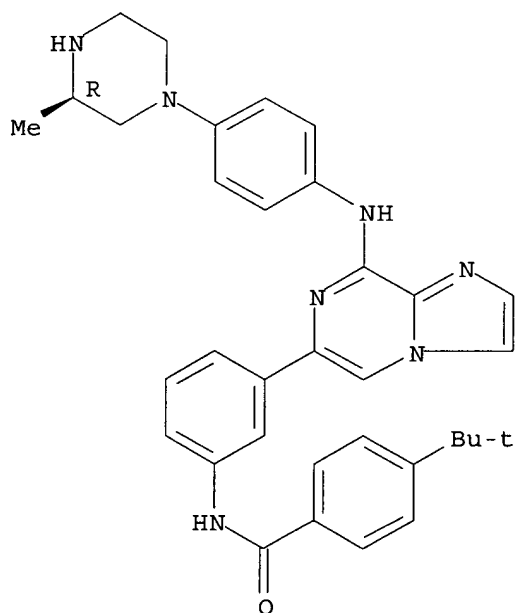
CN Benzoic acid, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-methyl-4-(1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-10-2 HCAPLUS

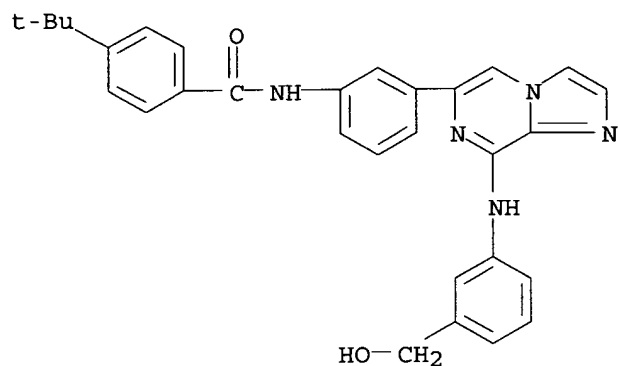
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3R)-3-methyl-1-piperazinyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 845270-11-3 HCAPLUS

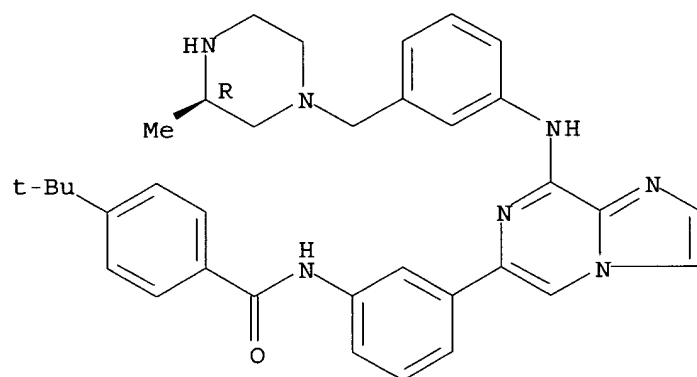
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-(hydroxymethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-12-4 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[[(3R)-3-methyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)

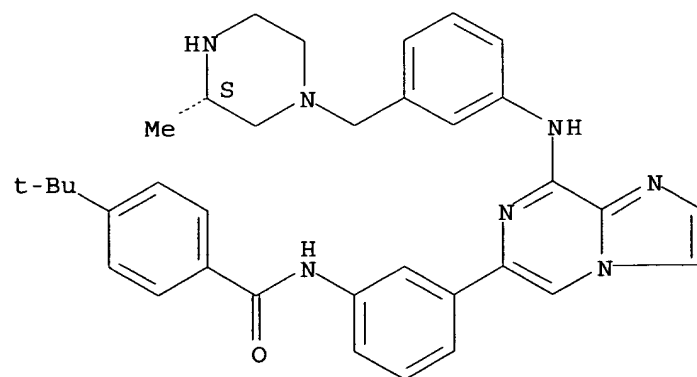
Absolute stereochemistry.



RN 845270-13-5 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[[(3S)-3-methyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)

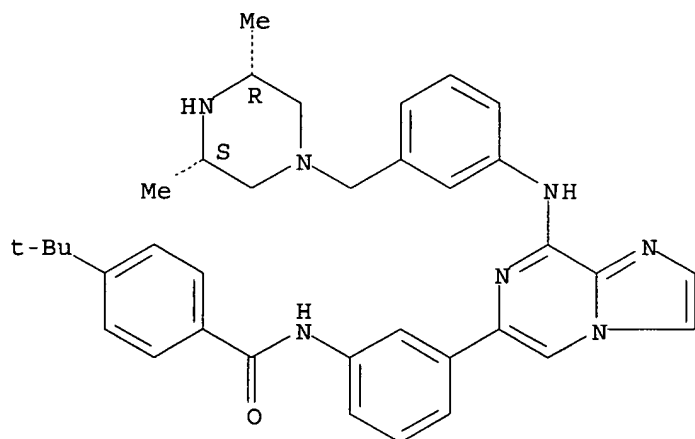
Absolute stereochemistry.



RN 845270-14-6 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[3-[[[(3R,5S)-3,5-dimethyl-1-piperazinyl]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-, rel-(9CI) (CA INDEX NAME)

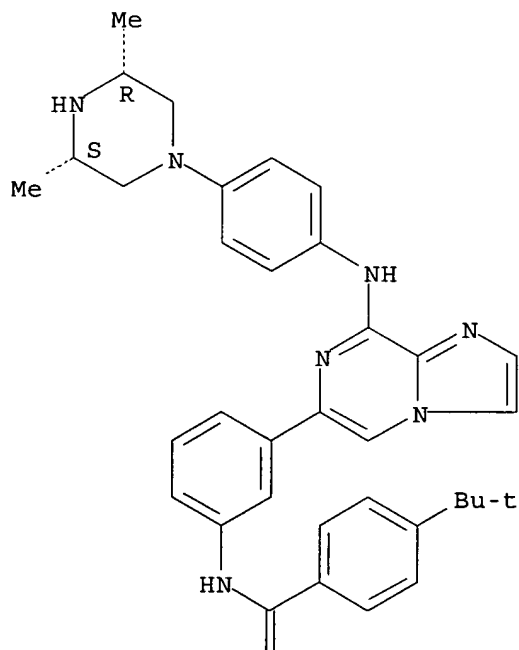
Relative stereochemistry.



RN 845270-15-7 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[[(3R,5S)-3,5-dimethyl-1-piperazinyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-, rel-(9CI) (CA INDEX NAME)

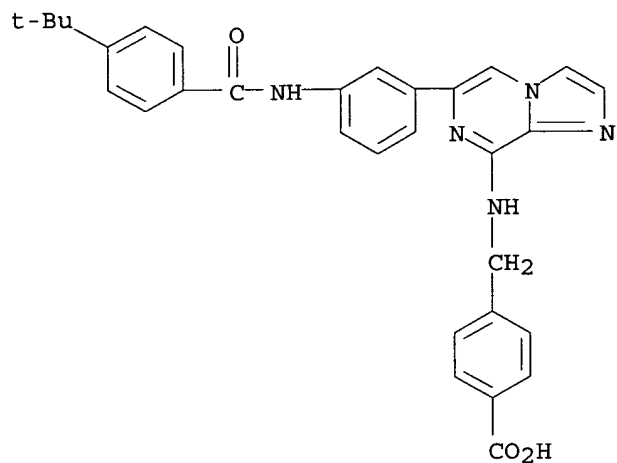
Relative stereochemistry.



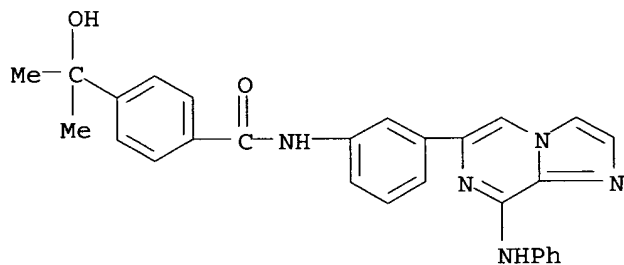
PAGE 1-A



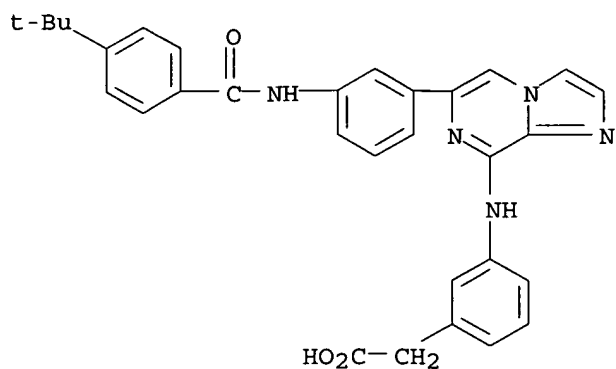
RN 845270-16-8 HCAPLUS
 CN Benzoic acid, 4-[[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]methyl]- (9CI) (CA INDEX NAME)



RN 845270-17-9 HCAPLUS
 CN Benzamide, 4-(1-hydroxy-1-methylethyl)-N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

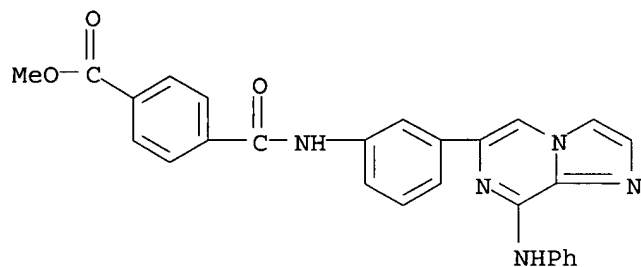


RN 845270-18-0 HCAPLUS
 CN Benzeneacetic acid, 3-[[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



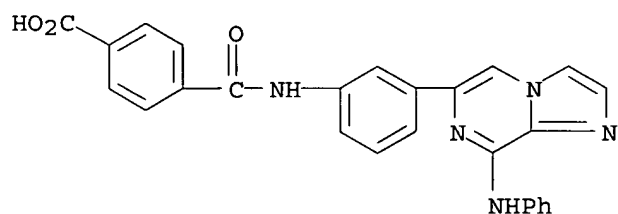
RN 845270-19-1 HCAPLUS

CN Benzoic acid, 4-[[[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



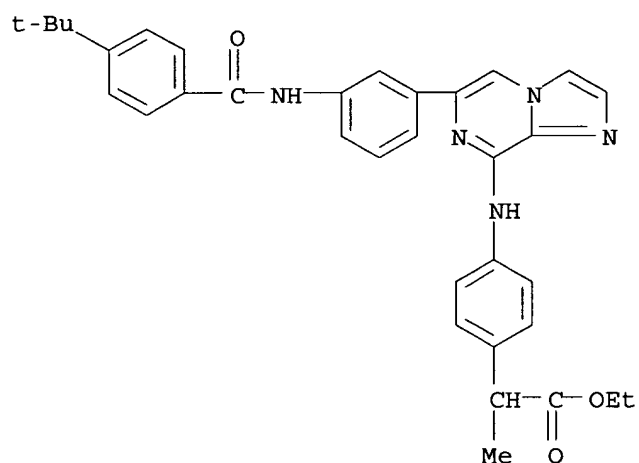
RN 845270-20-4 HCAPLUS

CN Benzoic acid, 4-[[[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



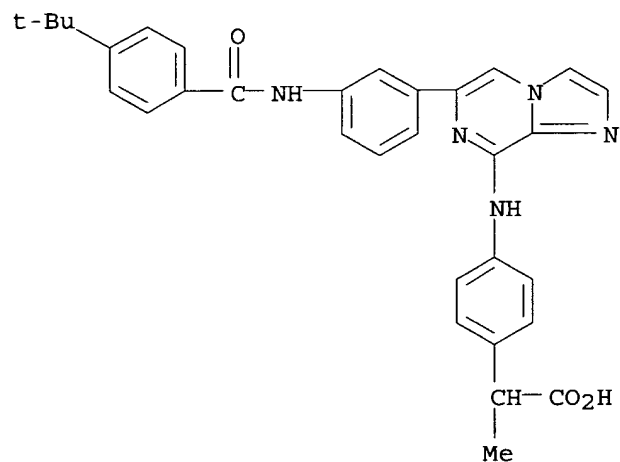
RN 845270-21-5 HCAPLUS

CN Benzeneacetic acid, 4-[[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-alpha-methyl]-, ethyl ester (9CI) (CA INDEX NAME)



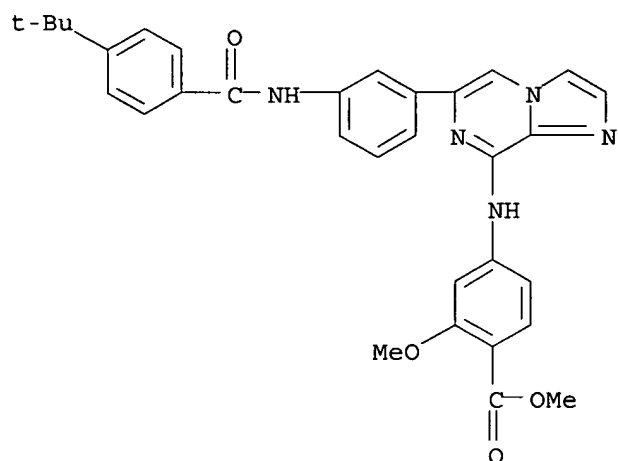
RN 845270-22-6 HCAPLUS

CN Benzeneacetic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-α-methyl- (9CI) (CA INDEX NAME)



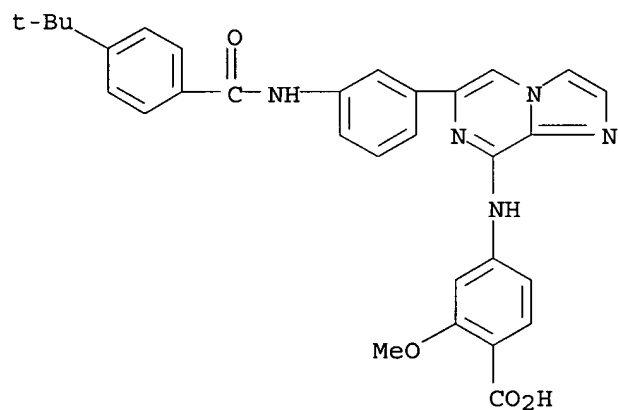
RN 845270-23-7 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methoxy-, methyl ester (9CI) (CA INDEX NAME)



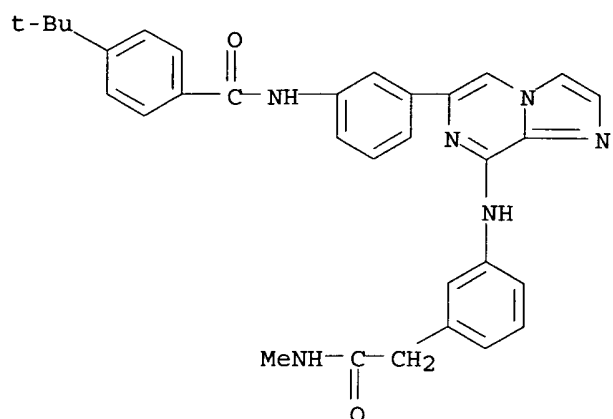
RN 845270-24-8 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-methoxy- (9CI) (CA INDEX NAME)



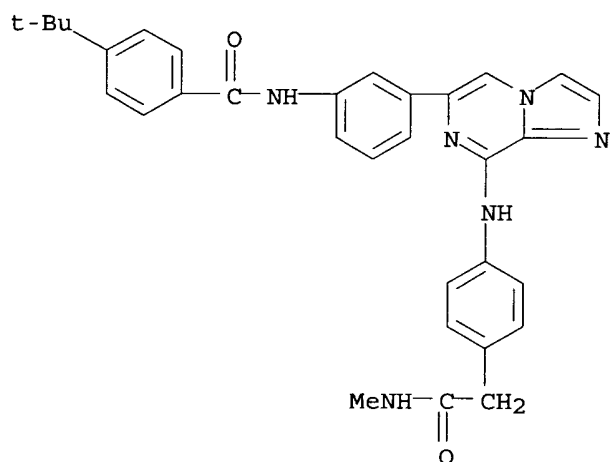
RN 845270-25-9 HCAPLUS

CN Benzeneacetamide, 3-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



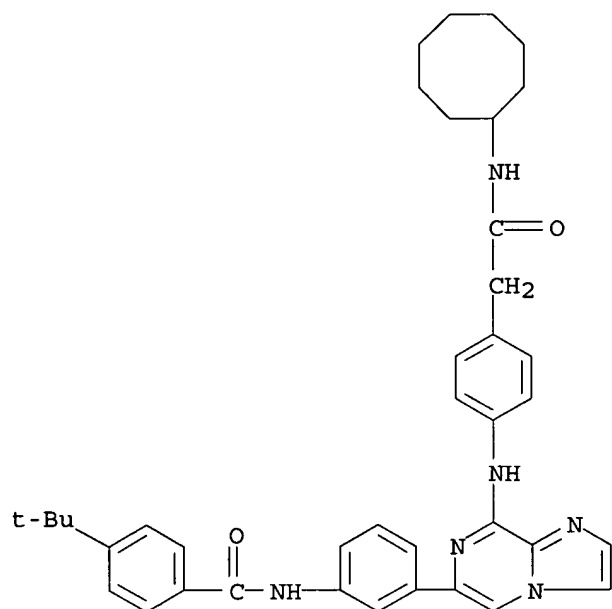
RN 845270-26-0 HCAPLUS

CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)



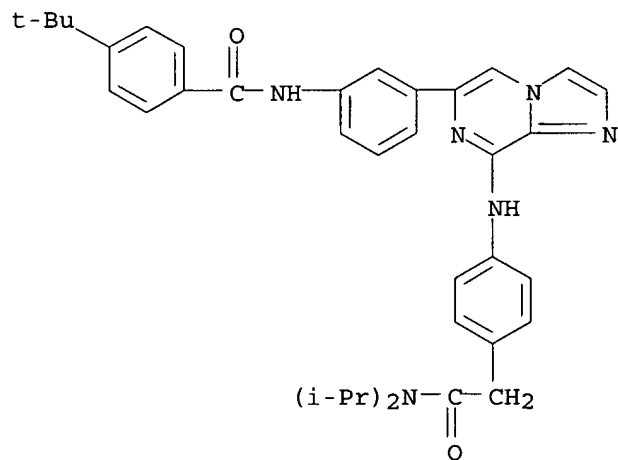
RN 845270-27-1 HCAPLUS

CN Benzeneacetamide, N-cyclooctyl-4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



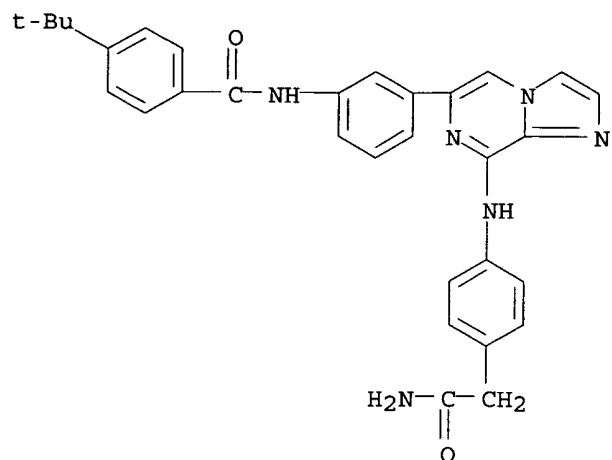
RN 845270-28-2 HCAPLUS

CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-bis(1-methylethyl)- (9CI) (CA INDEX NAME)

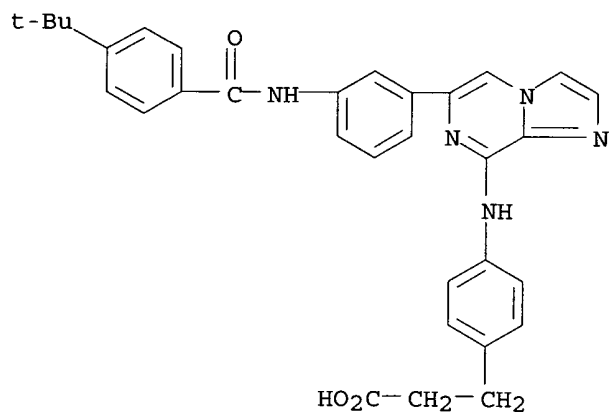


RN 845270-29-3 HCAPLUS

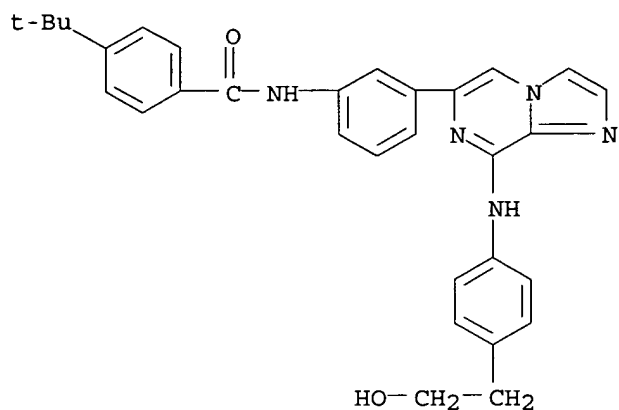
CN Benzeneacetamide, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)



RN 845270-30-6 HCAPLUS
 CN Benzenepropanoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI) (CA INDEX NAME)

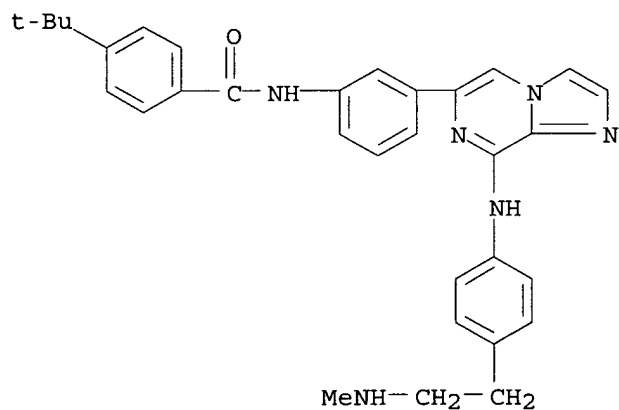


RN 845270-31-7 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(2-hydroxyethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



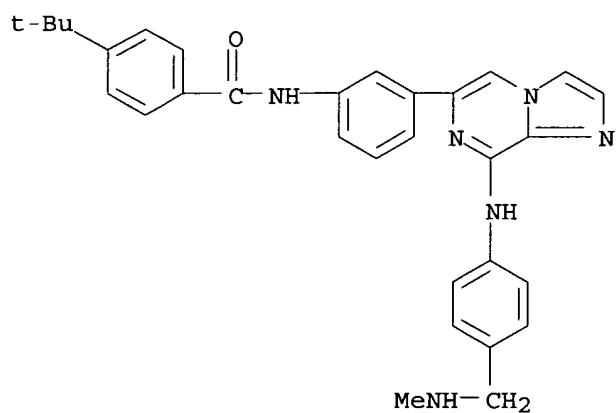
RN 845270-32-8 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(methylamino)ethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



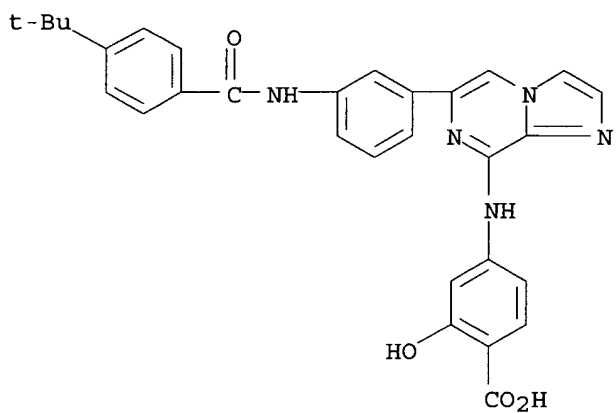
RN 845270-33-9 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



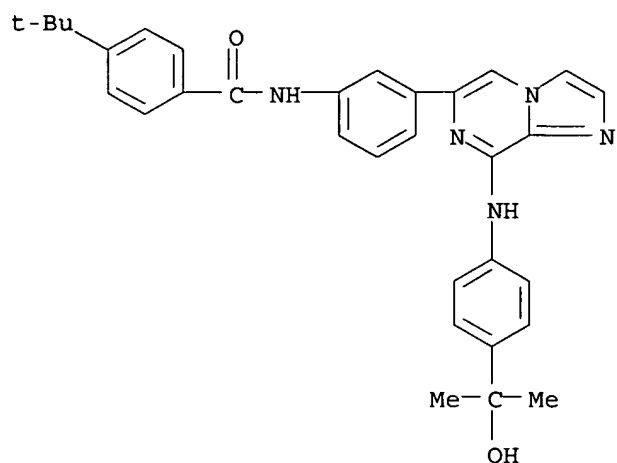
RN 845270-34-0 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)



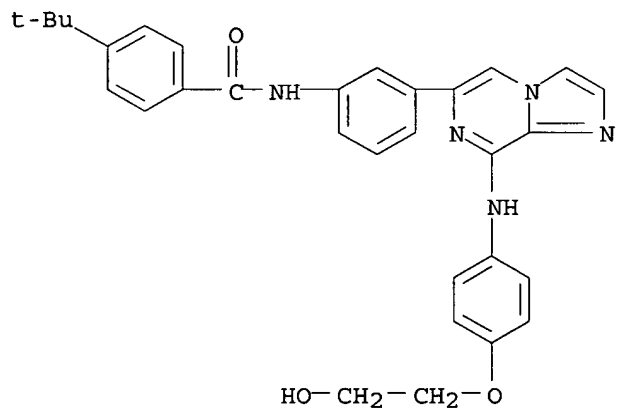
RN 845270-35-1 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-hydroxy-1-methylethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



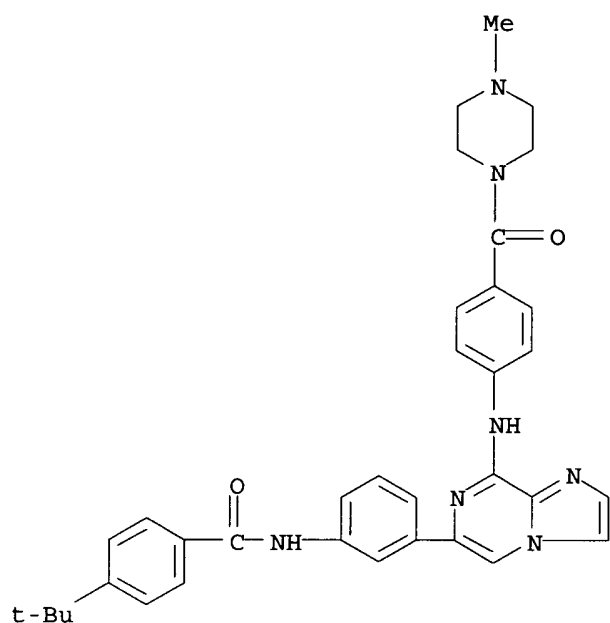
RN 845270-36-2 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(2-hydroxyethoxy)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



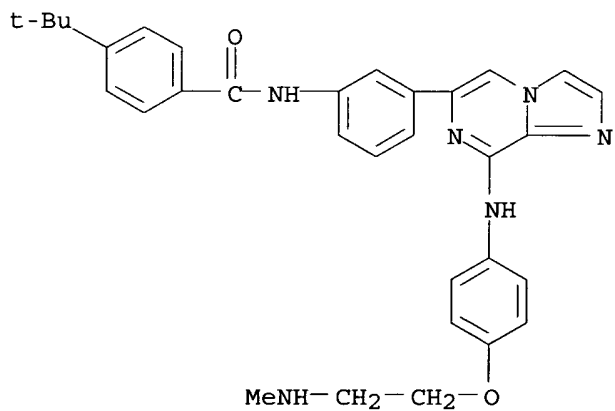
RN 845270-37-3 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



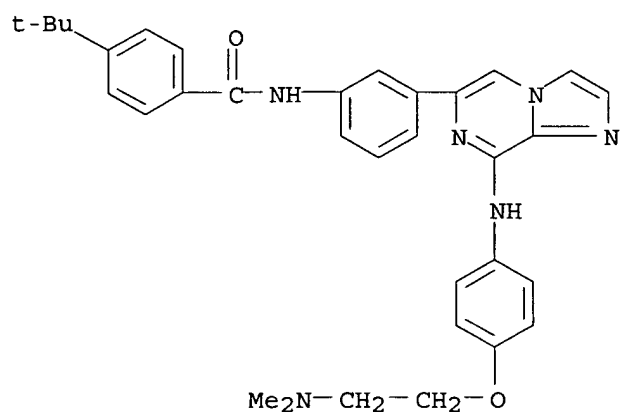
RN 845270-38-4 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(methylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



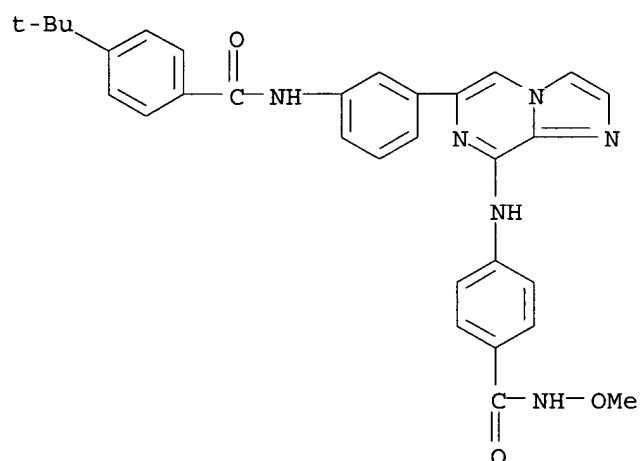
RN 845270-39-5 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[2-(dimethylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl) - (9CI) (CA INDEX NAME)



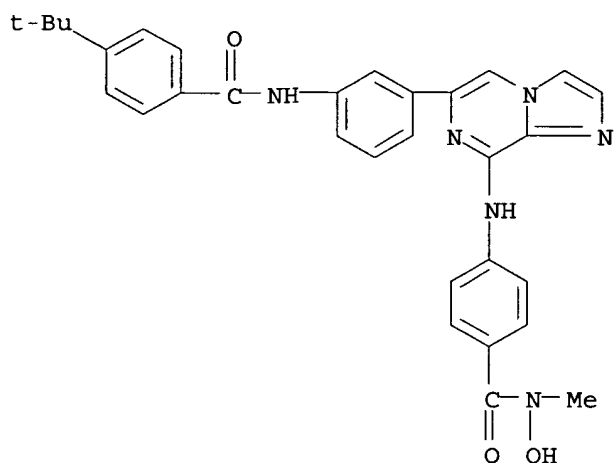
RN 845270-40-8 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methoxy- (9CI) (CA INDEX NAME)



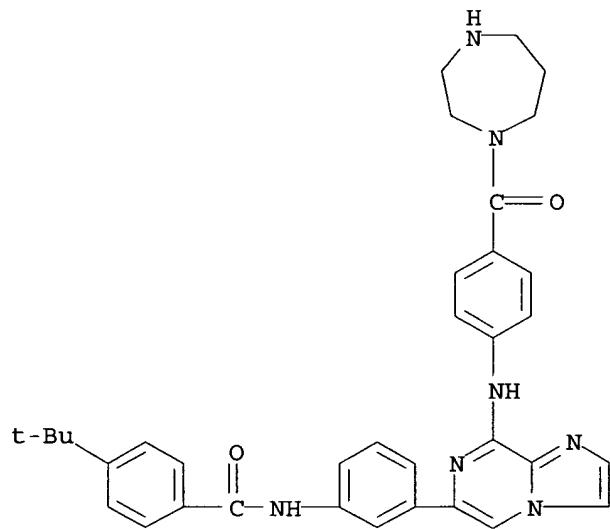
RN 845270-41-9 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-hydroxy-N-methyl- (9CI) (CA INDEX NAME)



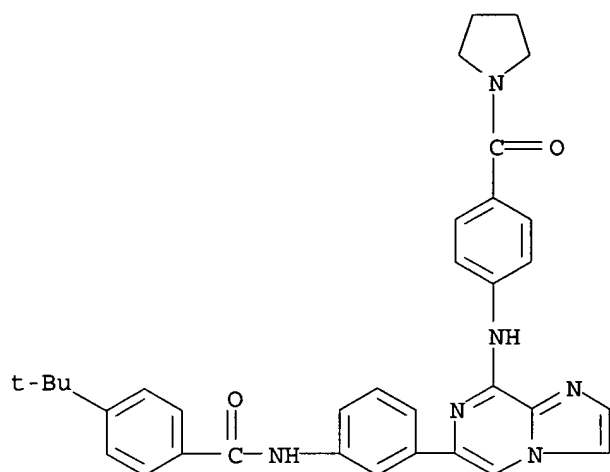
RN 845270-42-0 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[4-[4-(hexahydro-1H-1,4-diazepin-1-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



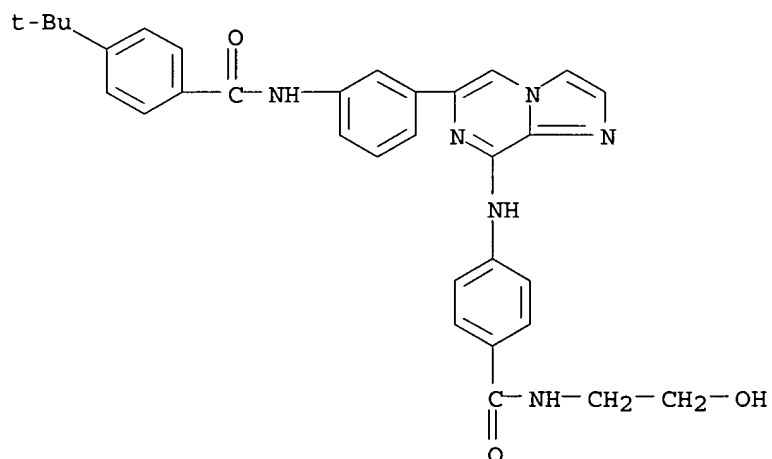
RN 845270-43-1 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[4-(1-pyrrolidinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



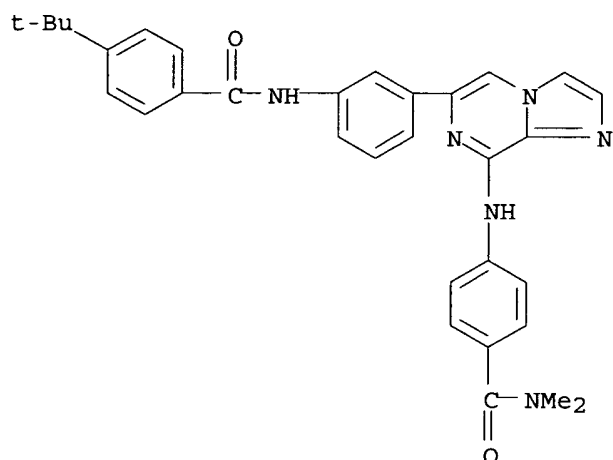
RN 845270-44-2 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



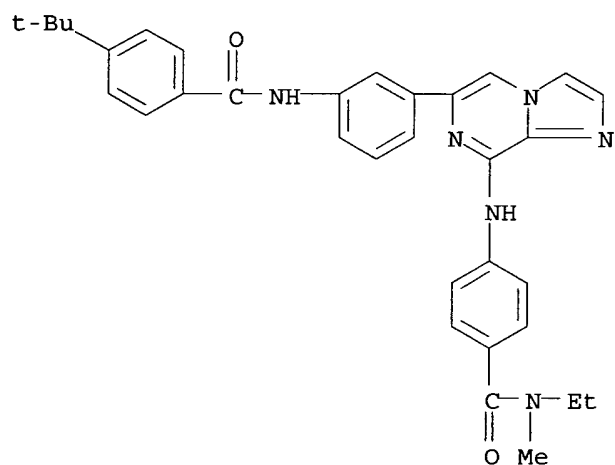
RN 845270-45-3 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N,N-dimethyl- (9CI) (CA INDEX NAME)



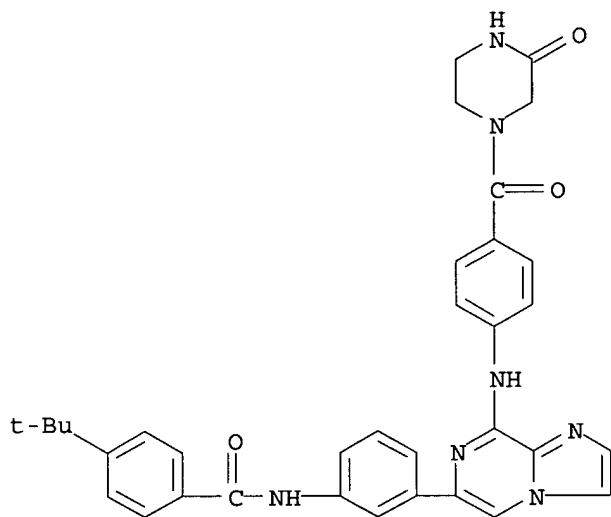
RN 845270-46-4 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-ethyl-N-methyl- (9CI) (CA INDEX NAME)



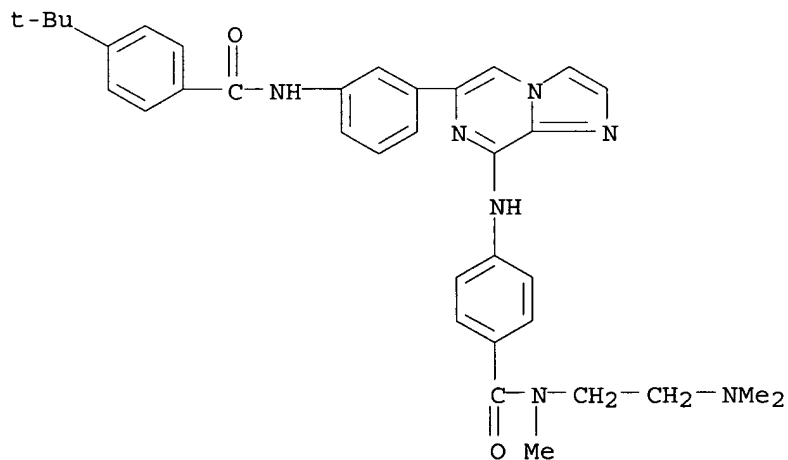
RN 845270-47-5 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



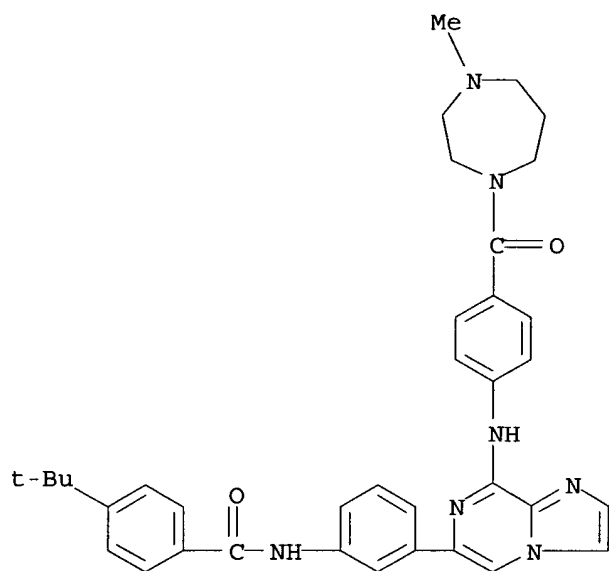
RN 845270-48-6 HCAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-methyl- (9CI) (CA INDEX NAME)

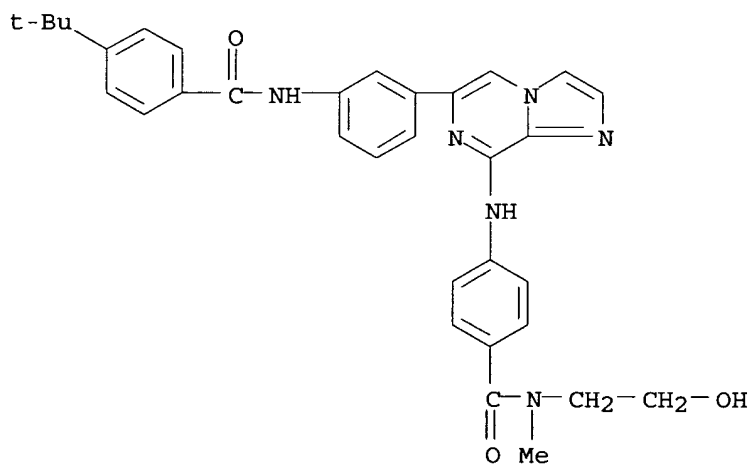


RN 845270-49-7 HCAPLUS

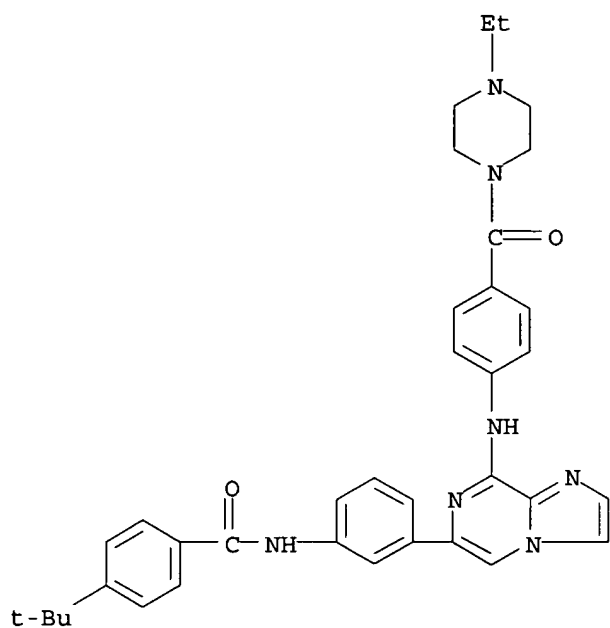
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-50-0 HCAPLUS
 CN Benzamide, 4-[[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(2-hydroxyethyl)-N-methyl- (9CI) (CA INDEX NAME)

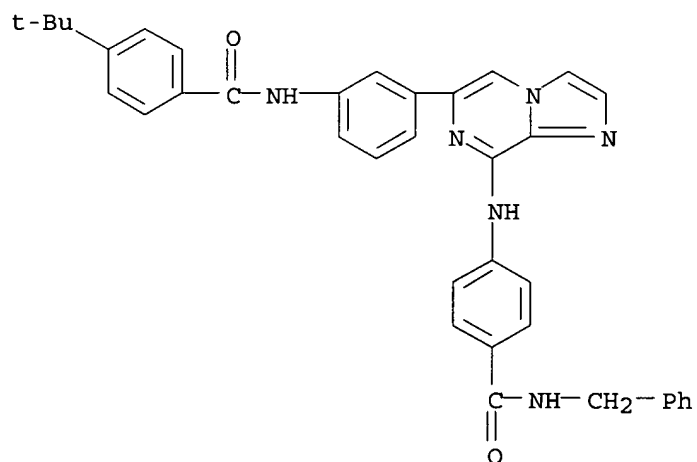


RN 845270-51-1 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-ethyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



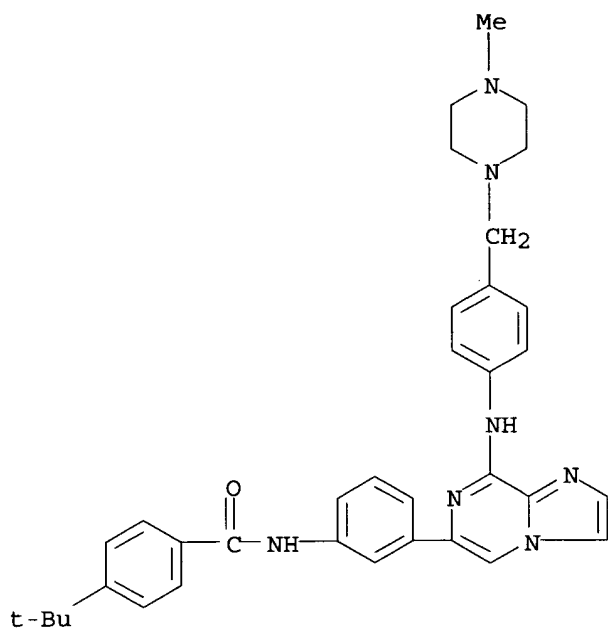
RN 845270-52-2 HCAPLUS

CN Benzamide, 4-[[6-[[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



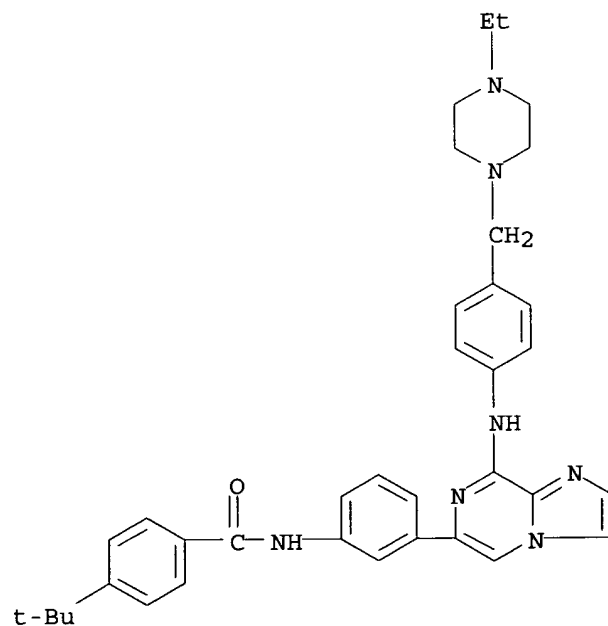
RN 845270-54-4 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-methyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



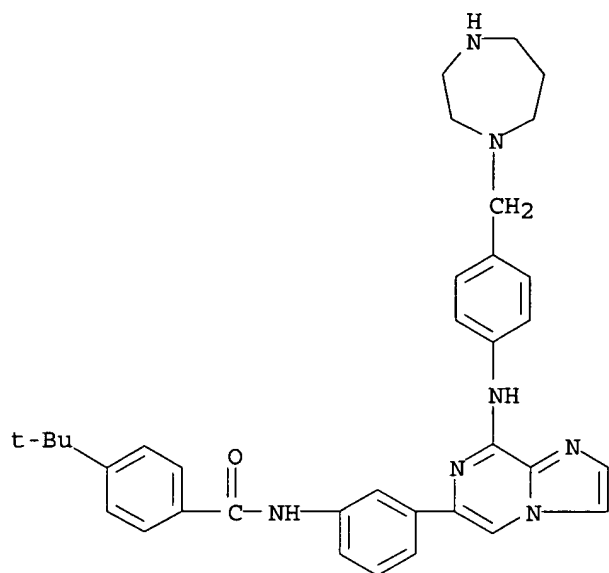
RN 845270-56-6 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(4-ethyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



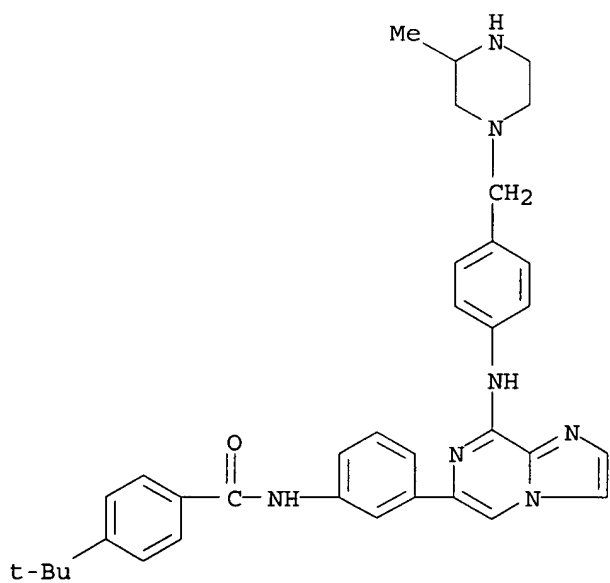
RN 845270-57-7 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-1H-1,4-diazepin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



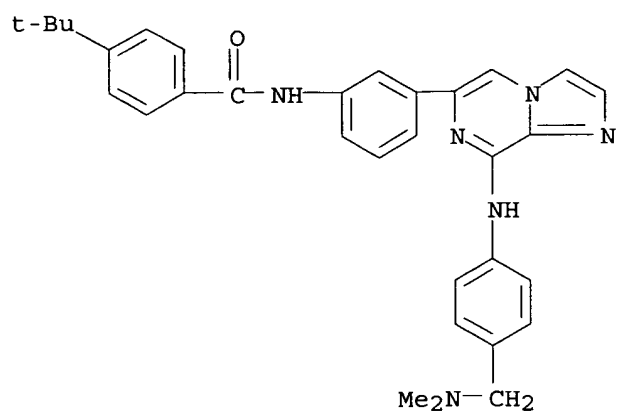
RN 845270-58-8 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-methyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



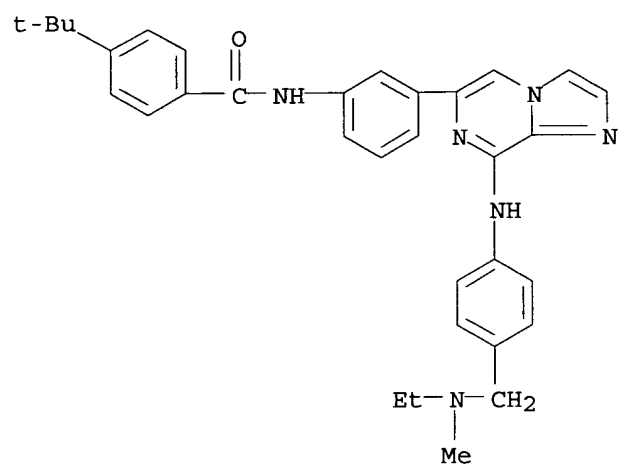
RN 845270-59-9 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[(dimethylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



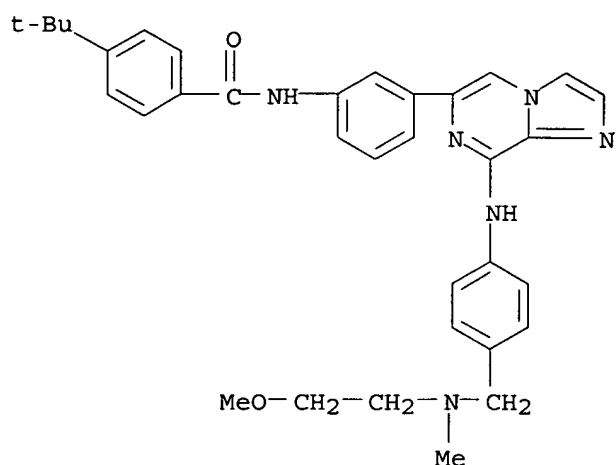
RN 845270-60-2 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(ethylmethyamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



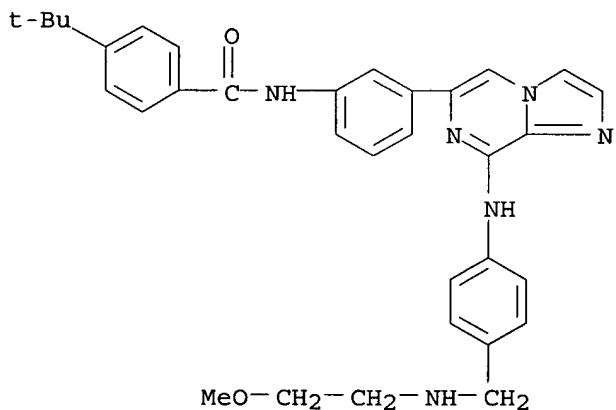
RN 845270-61-3 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[2-methoxyethyl)methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



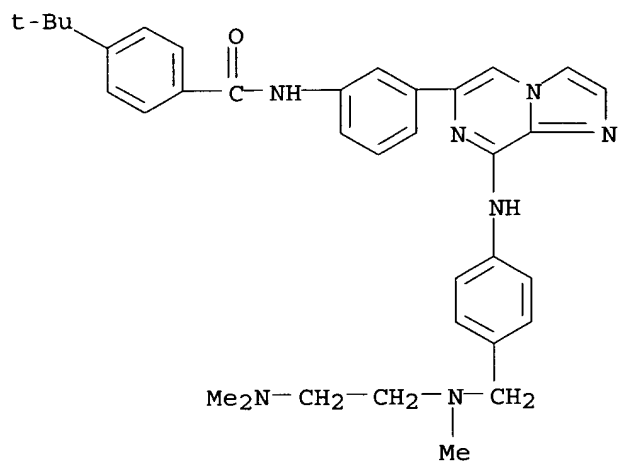
RN 845270-62-4 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[2-methoxyethyl]amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)

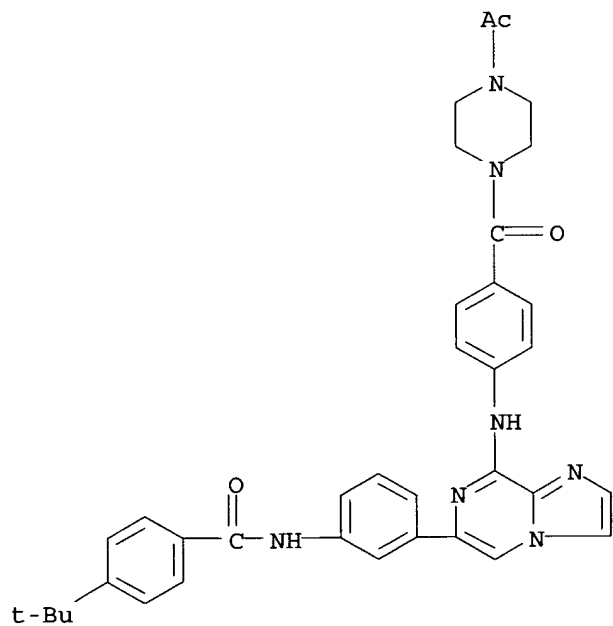


RN 845270-63-5 HCAPLUS

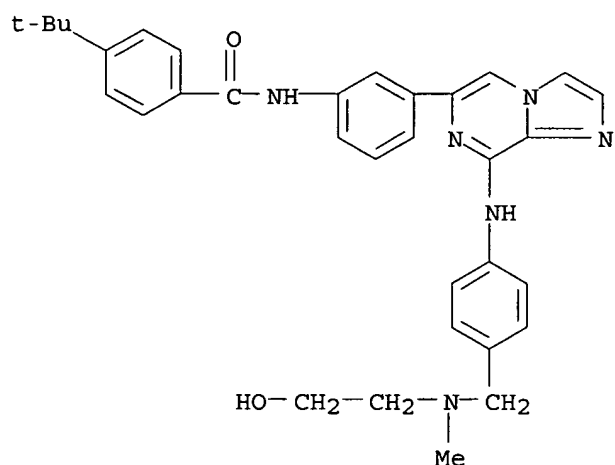
CN Benzamide, N-[3-[8-[[4-[[2-(dimethylamino)ethyl]methylamino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)-(9CI) (CA INDEX NAME)



RN 845270-64-6 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

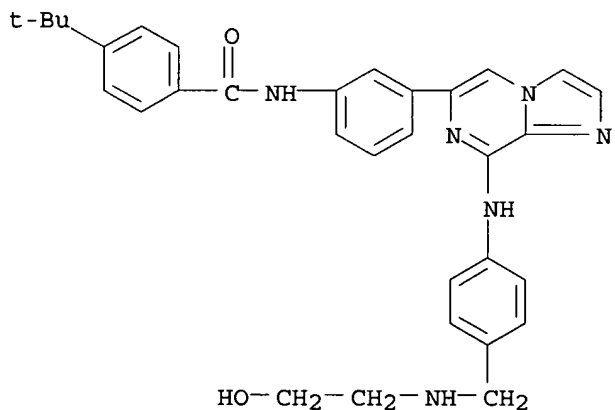


RN 845270-65-7 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[[2-hydroxyethyl)methylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



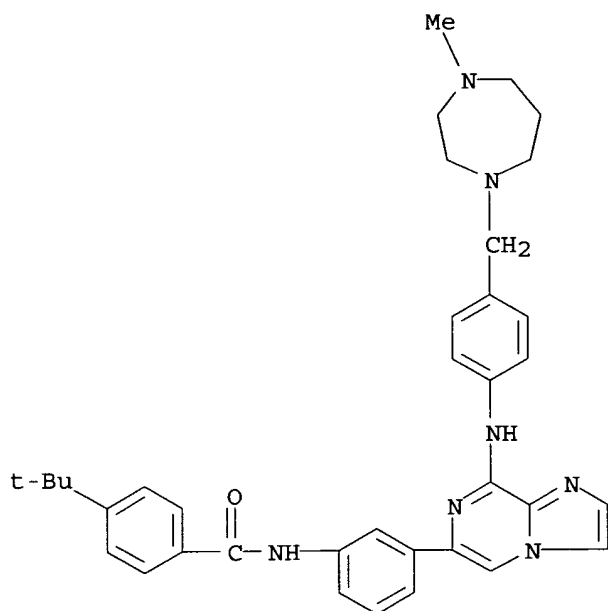
RN 845270-66-8 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[2-hydroxyethyl)amino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



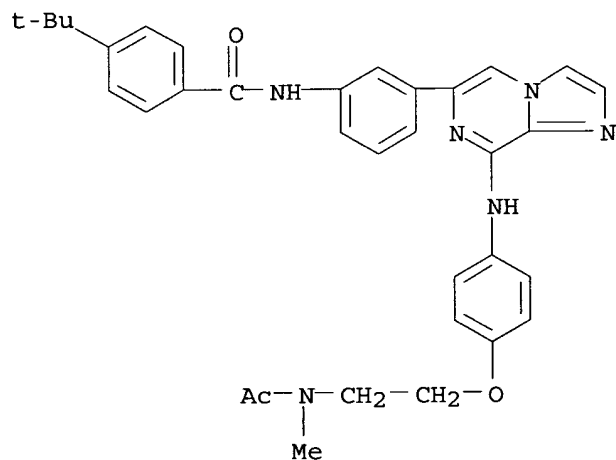
RN 845270-67-9 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



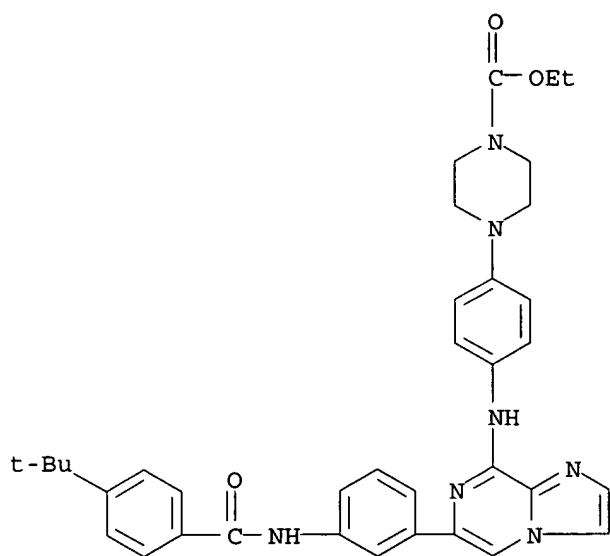
RN 845270-68-0 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[2-(acetylmethylamino)ethoxy]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



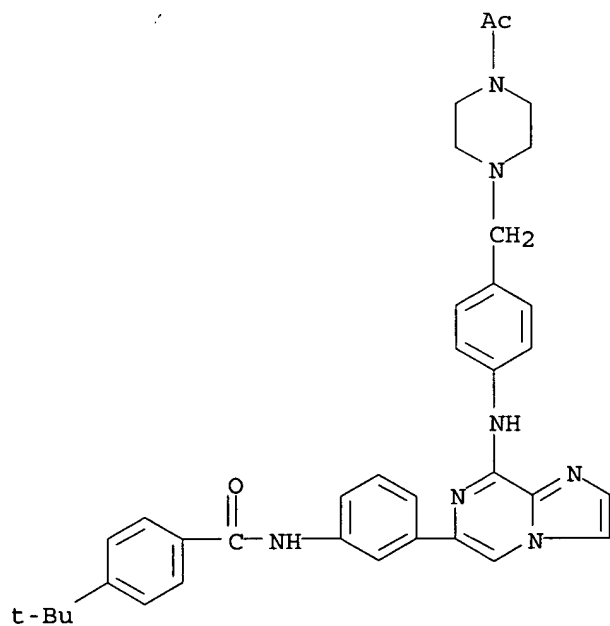
RN 845270-69-1 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



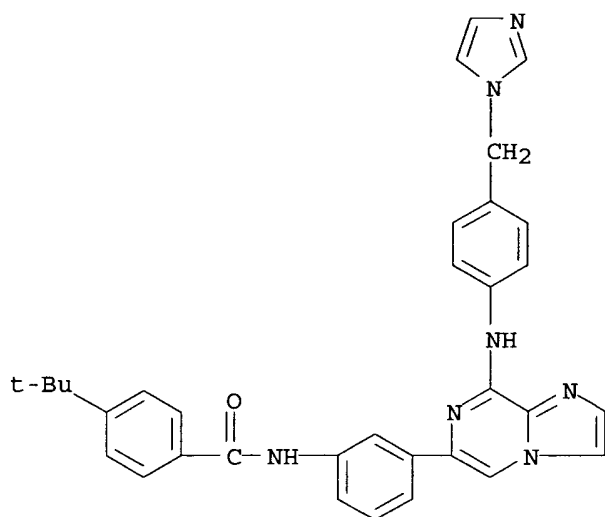
RN 845270-70-4 HCAPLUS

CN Benzamide, N- [3- [8- [[4- [(4-acetyl-1-piperazinyl)methyl]phenyl]amino]imidazo
o[1,2-a]pyrazin-6-yl]phenyl]-4- (1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



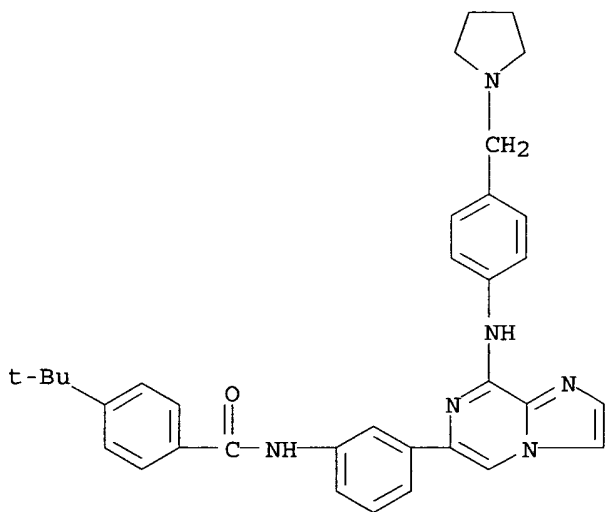
RN 845270-71-5 HCAPLUS

CN Benzamide, 4- (1,1-dimethylethyl)-N- [3- [8- [[4- (1H-imidazol-1-
ylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX
NAME)



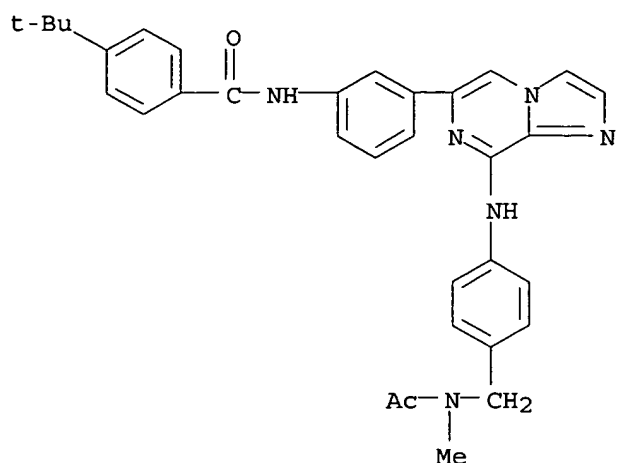
RN 845270-72-6 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(1-pyrrolidinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)



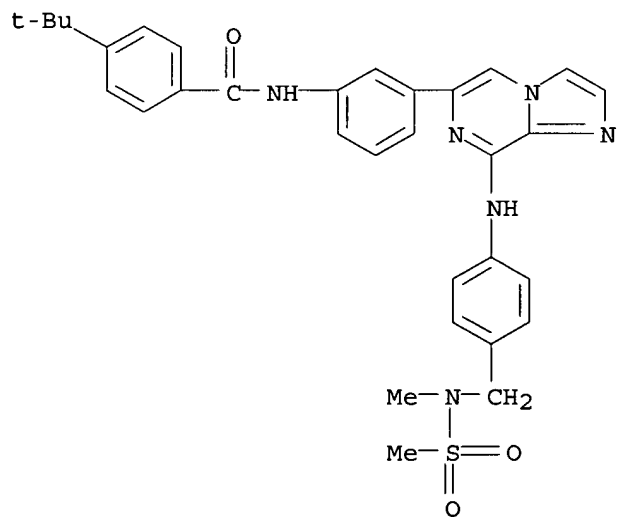
RN 845270-73-7 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[(acetylmethylamino)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



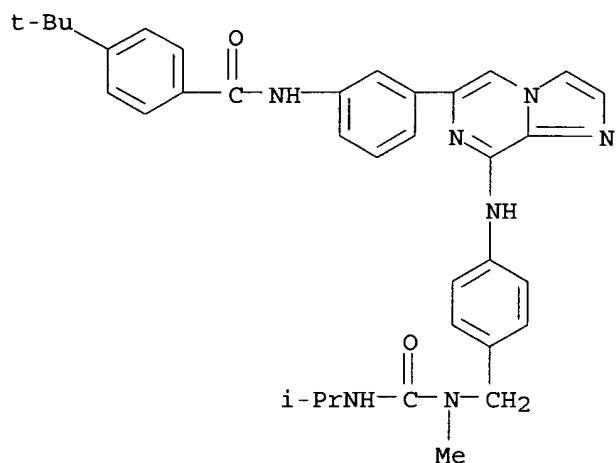
RN 845270-74-8 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[methyl(methylsulfonyl)amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



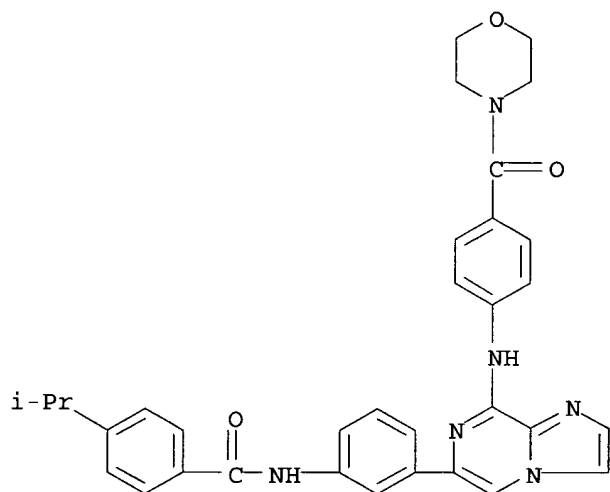
RN 845270-75-9 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[[methyl[(1-methylethyl)amino]carbonyl]amino]methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



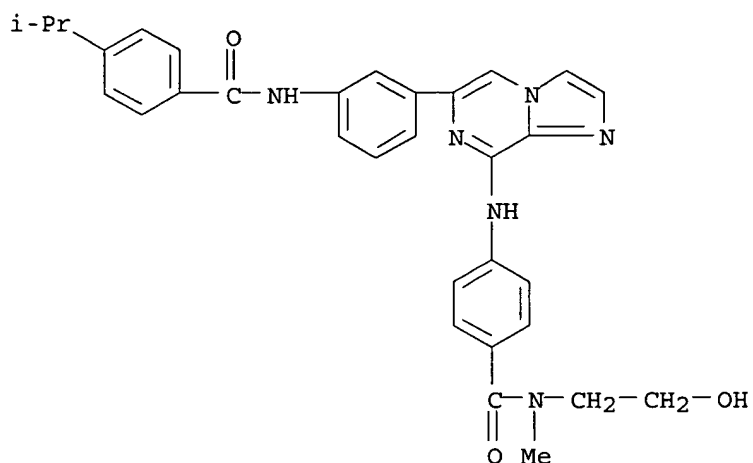
RN 845270-77-1 HCAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



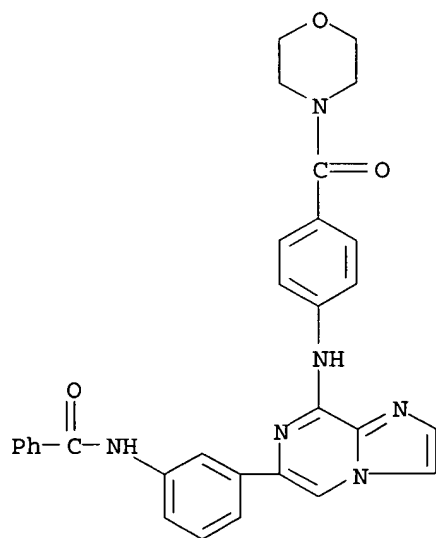
RN 845270-78-2 HCAPLUS

CN Benzamide, N-(2-hydroxyethyl)-N-methyl-4-[[6-[3-[[4-(1-methylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



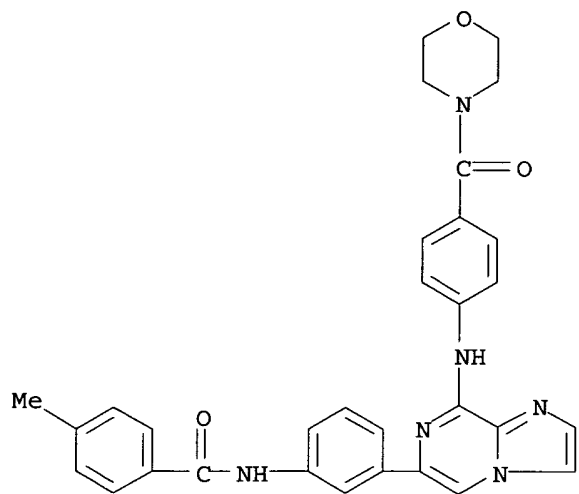
RN 845270-79-3 HCAPLUS

CN Benzamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



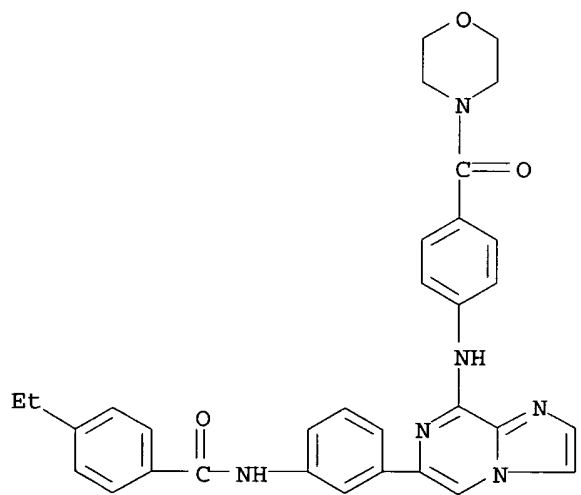
RN 845270-80-6 HCAPLUS

CN Benzamide, 4-methyl-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



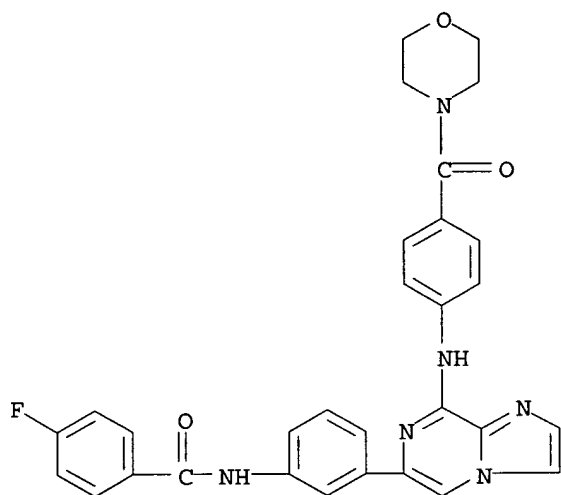
RN 845270-81-7 HCAPLUS

CN Benzamide, 4-ethyl-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo
[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

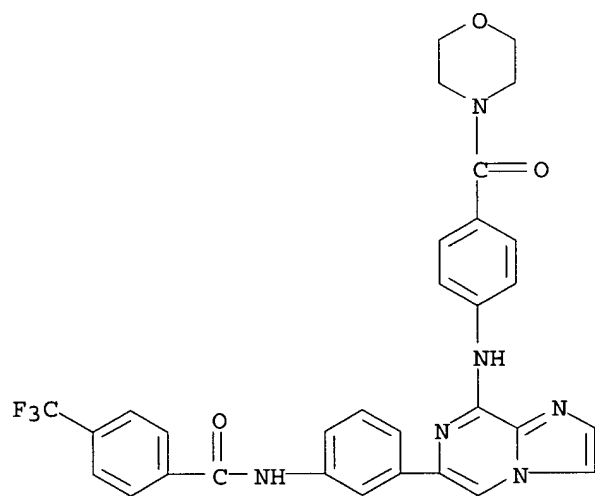


RN 845270-82-8 HCAPLUS

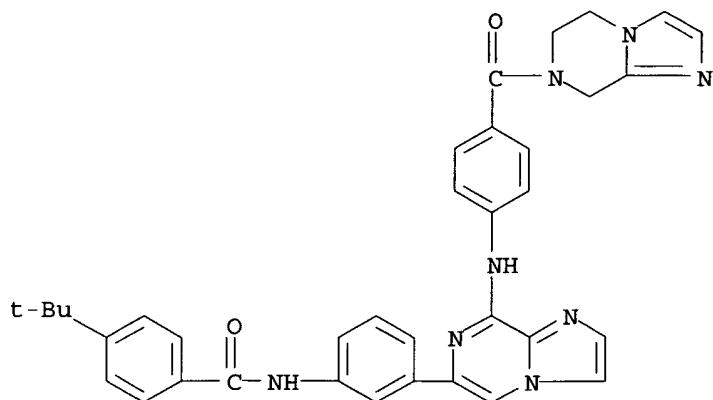
CN Benzamide, 4-fluoro-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidaz
o[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 845270-83-9 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)

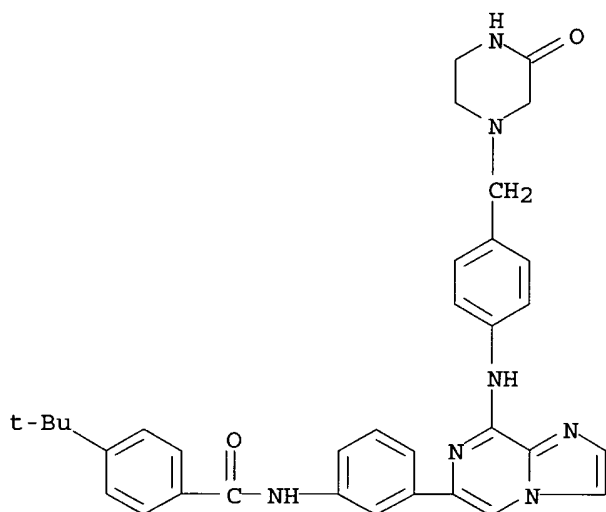


RN 845270-84-0 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-[(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 845270-85-1 HCAPLUS

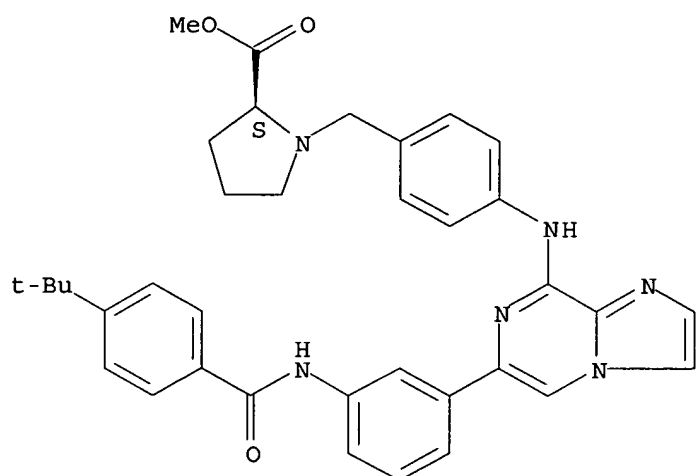
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



RN 845270-86-2 HCAPLUS

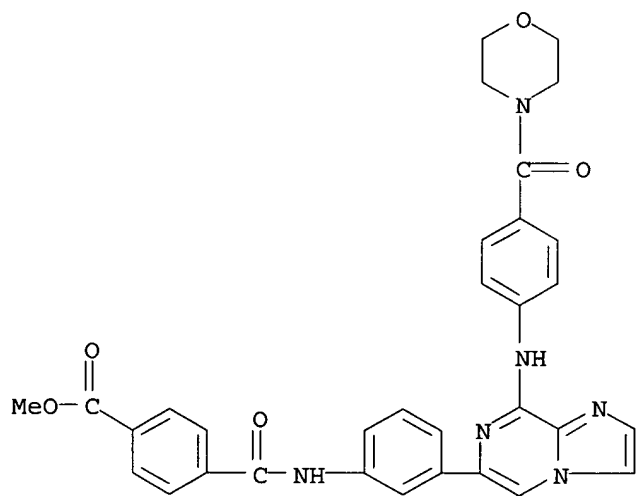
CN L-Proline, 1-[[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



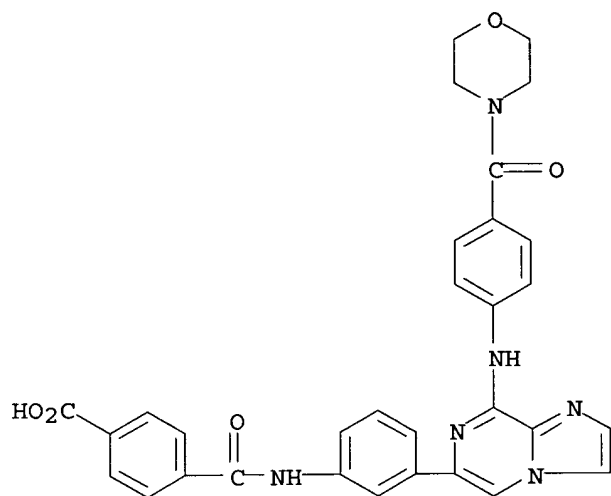
RN 845270-87-3 HCAPLUS

CN Benzoic acid, 4-[[[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

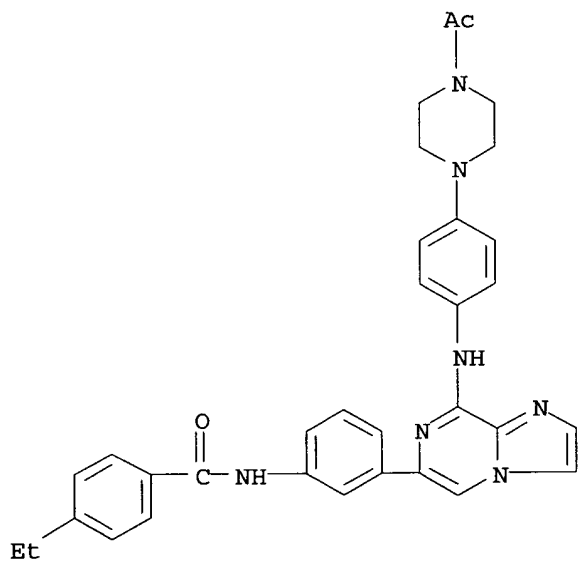


RN 845270-88-4 HCAPLUS

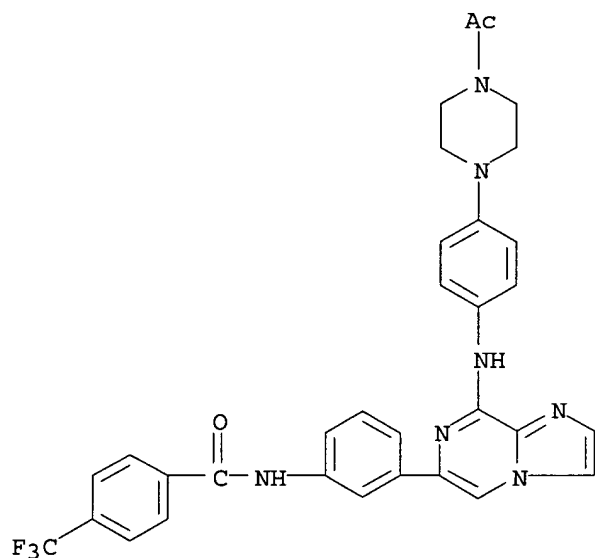
CN Benzoic acid, 4-[[[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



RN 845270-89-5 HCAPLUS
 CN Benzamide, N-[3-[8-[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-ethyl- (9CI) (CA INDEX NAME)

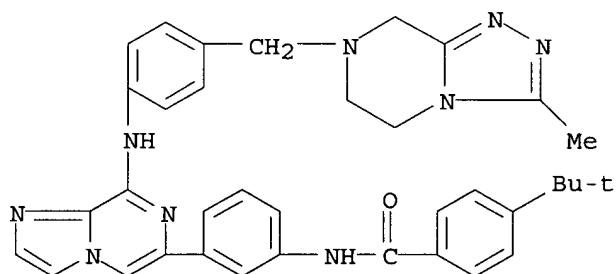


RN 845270-90-8 HCAPLUS
 CN Benzamide, N-[3-[8-[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



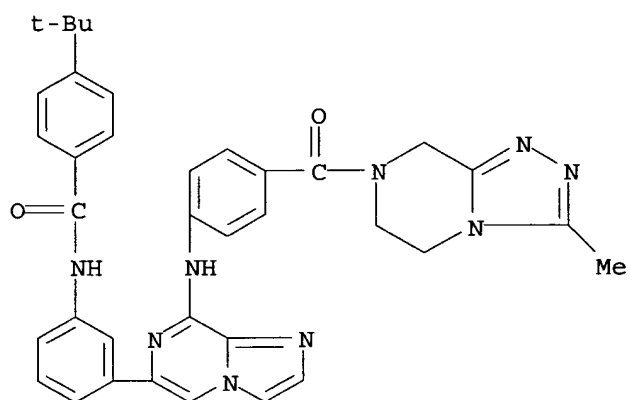
RN 845270-91-9 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



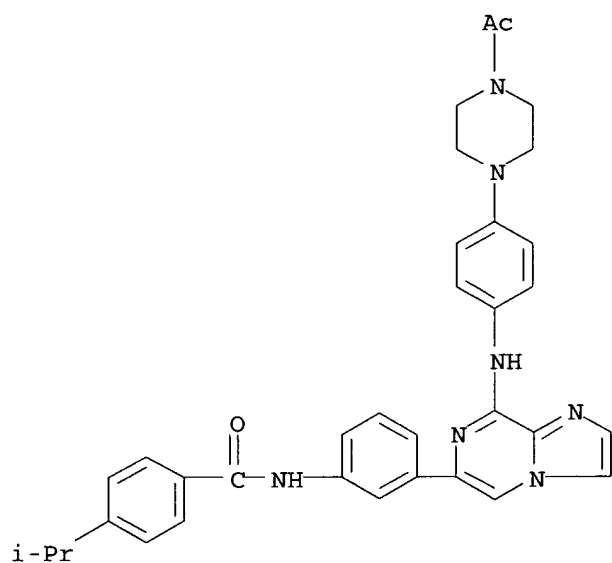
RN 845270-92-0 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



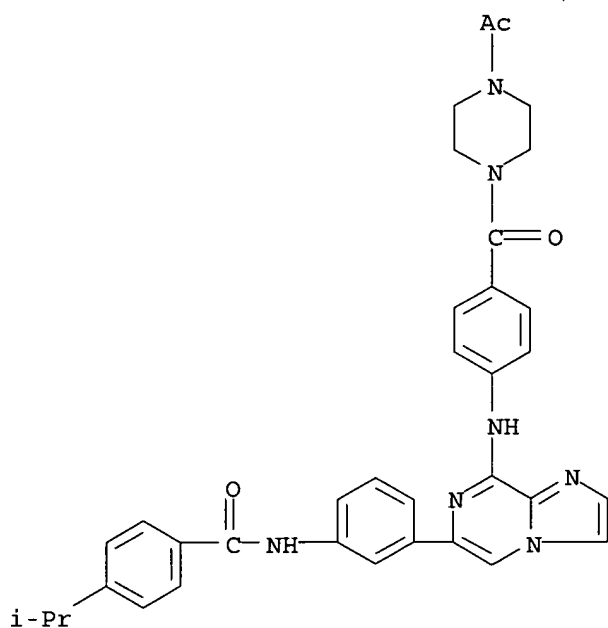
RN 845270-93-1 HCAPLUS

CN Benzamide, N-[3-[8-[[4-(4-acetyl-1-piperazinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 845270-94-2 HCAPLUS

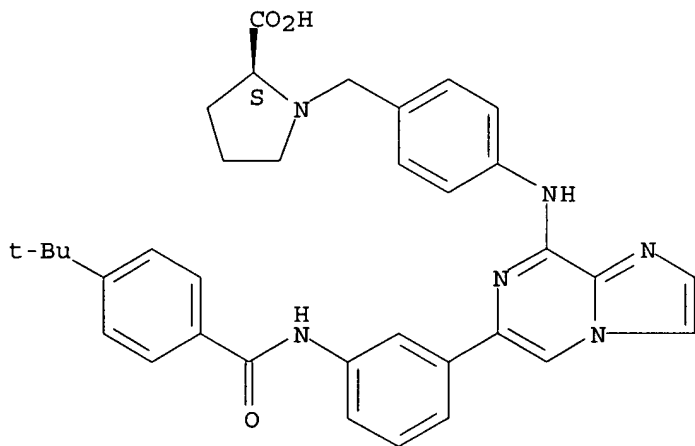
CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 845270-95-3 HCAPLUS

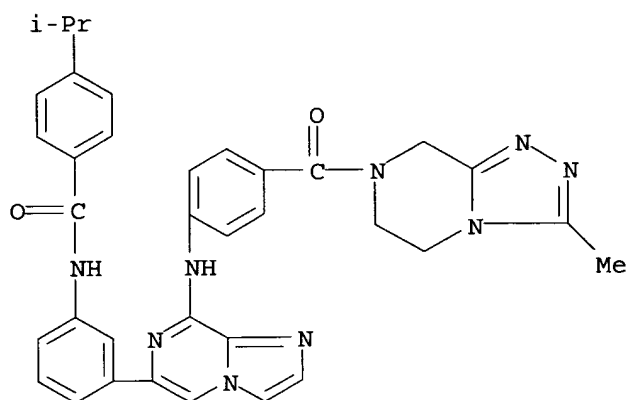
CN L-Proline, 1-[[4-[[6-[3-[[4-(1,1-dimethylethyl)benzoyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



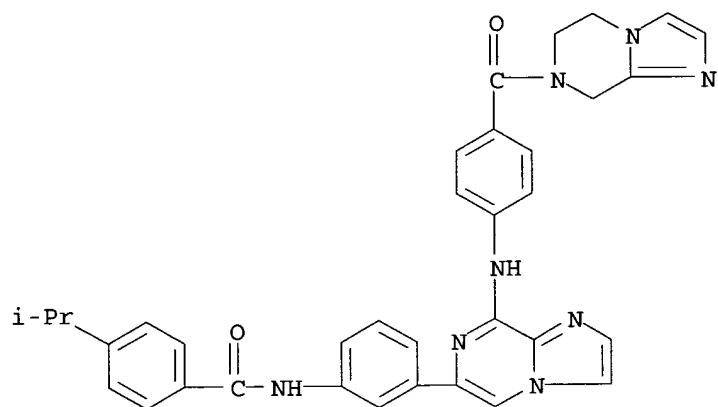
RN 845270-96-4 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[[5,6-dihydro-3-methyl-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



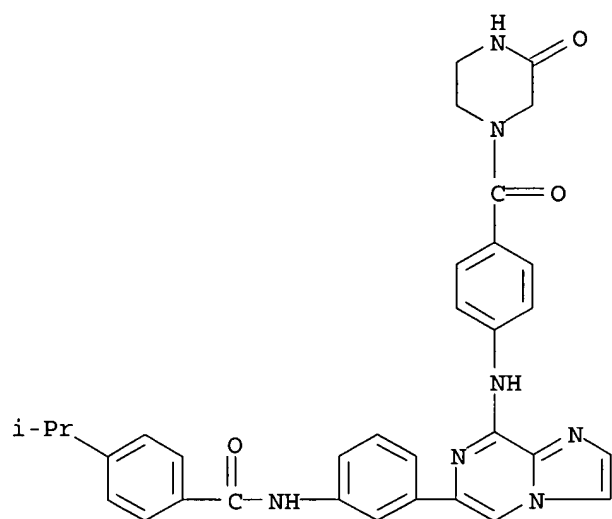
RN 845270-97-5 HCAPLUS

CN Benzamide, N-[3-[8-[[4-[(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)



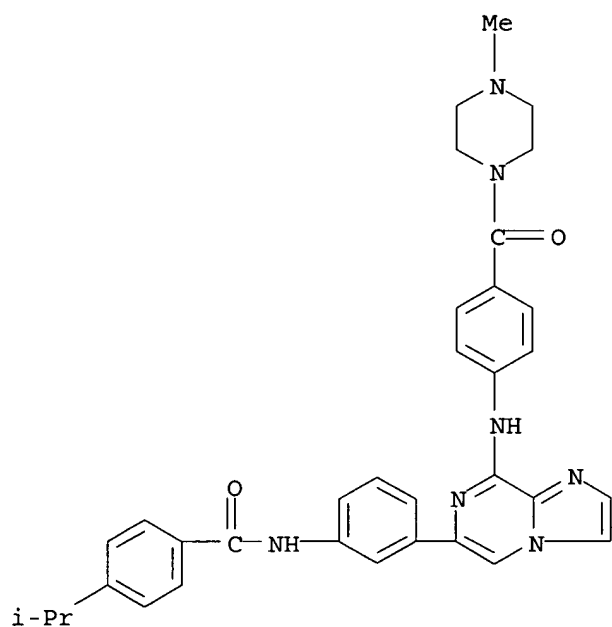
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CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



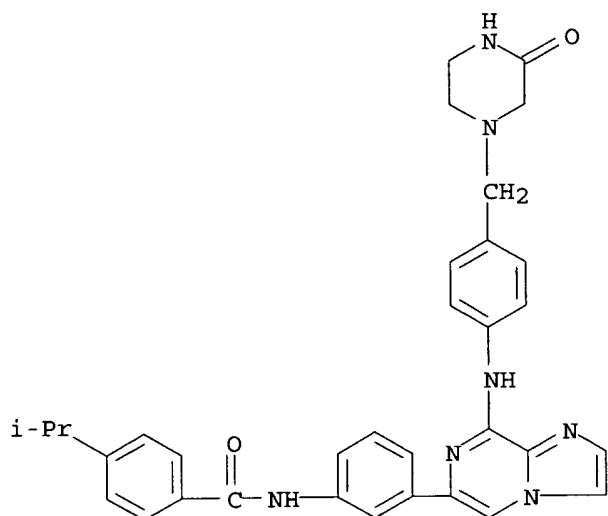
RN 845270-99-7 HCAPLUS

CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(4-methyl-1-piperazinyl)carbonyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)

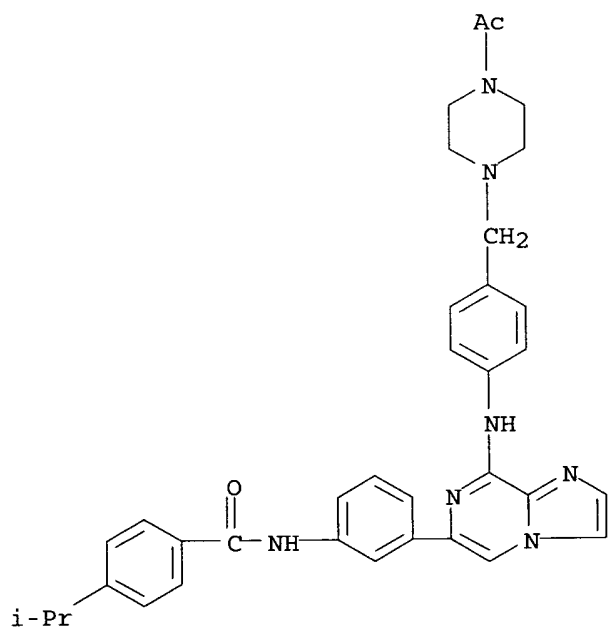


RN 845271-00-3 HCAPLUS

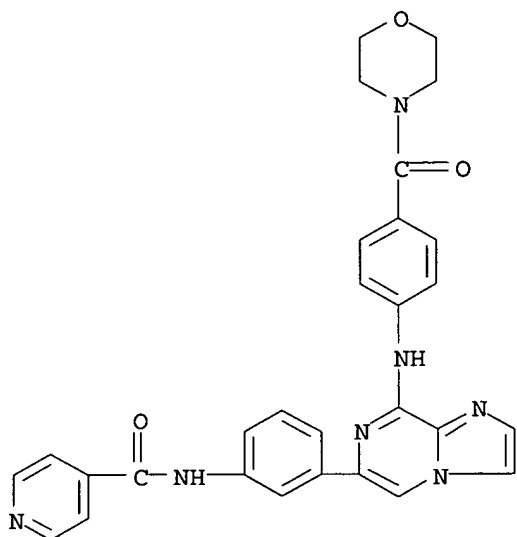
CN Benzamide, 4-(1-methylethyl)-N-[3-[8-[[4-[(3-oxo-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-(9CI) (CA INDEX NAME)



RN 845271-01-4 HCAPLUS
 CN Benzamide, N-[3-[8-[[4-[(4-acetyl-1-piperazinyl)methyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1-methylethyl)- (9CI) (CA INDEX NAME)

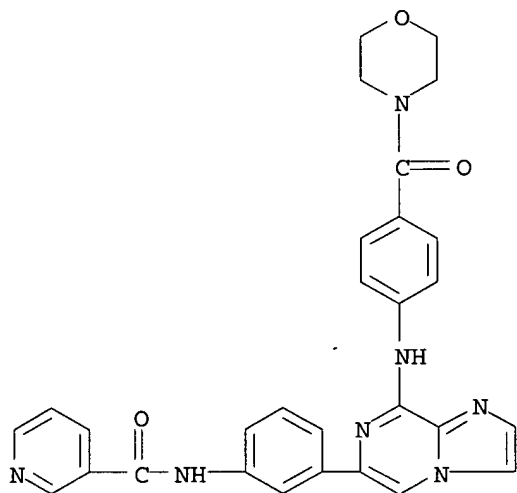


RN 845271-03-6 HCAPLUS
 CN 4-Pyridinecarboxamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



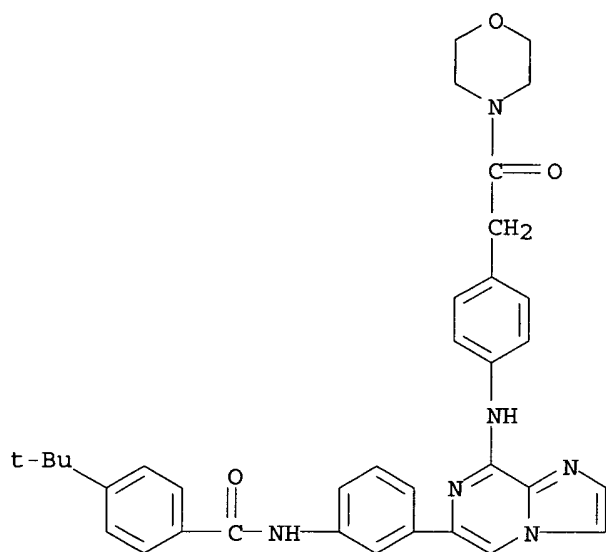
RN 845271-05-8 HCAPLUS

CN 3-Pyridinecarboxamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



RN 845271-07-0 HCAPLUS

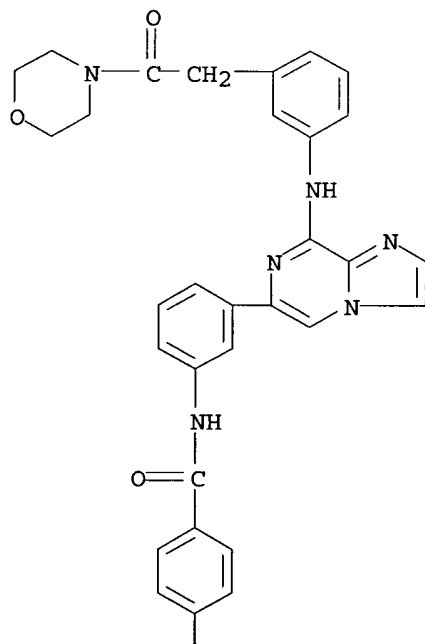
CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-[2-(4-morpholinyl)-2-oxoethyl]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



RN 845271-09-2 HCAPLUS

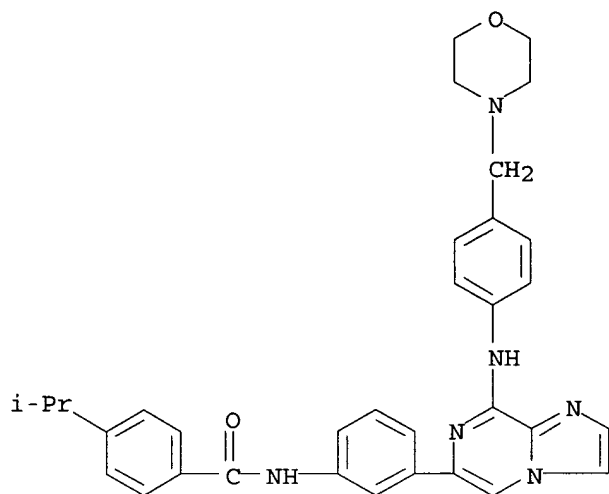
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PAGE 1-A

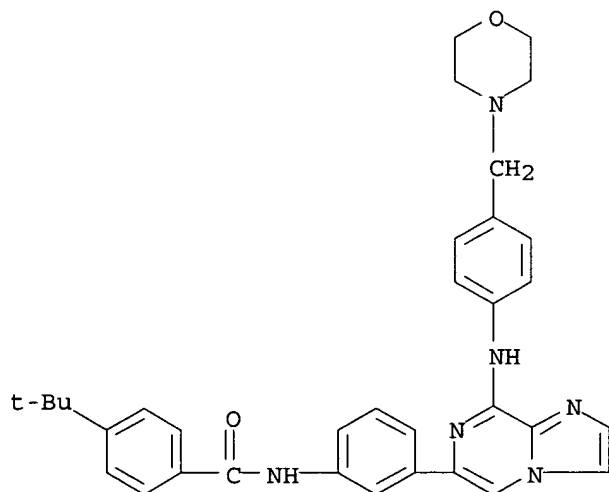




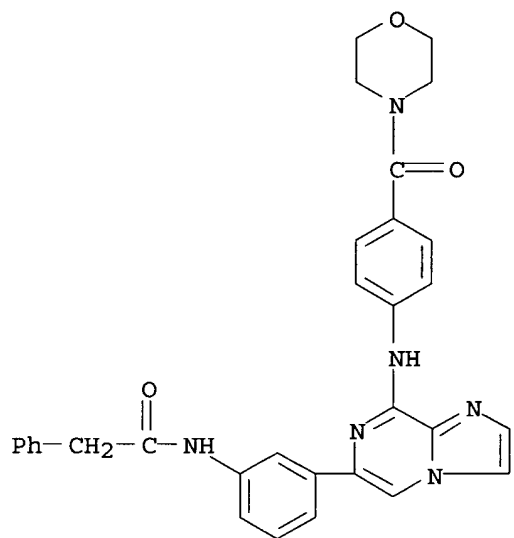
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RN 845271-13-8 HCAPLUS
 CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-morpholinylmethyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

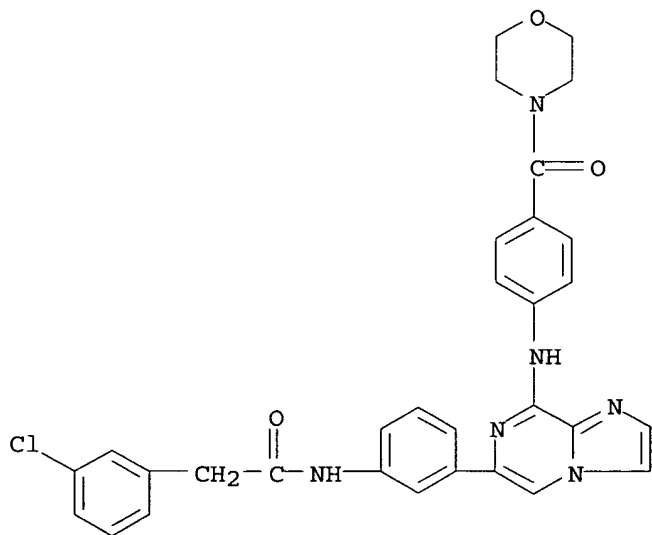


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 CN Benzeneacetamide, N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



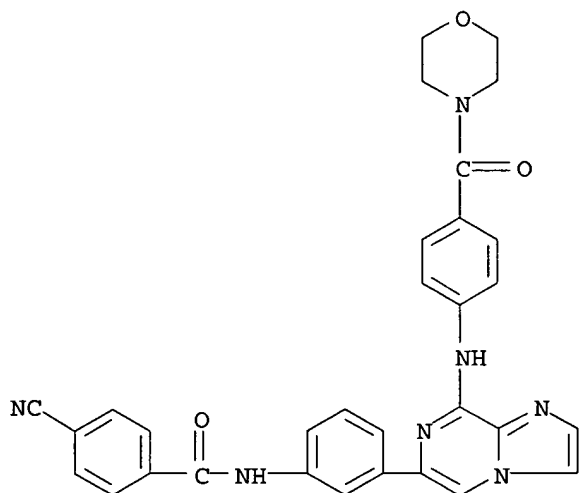
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CN Benzeneacetamide, 3-chloro-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



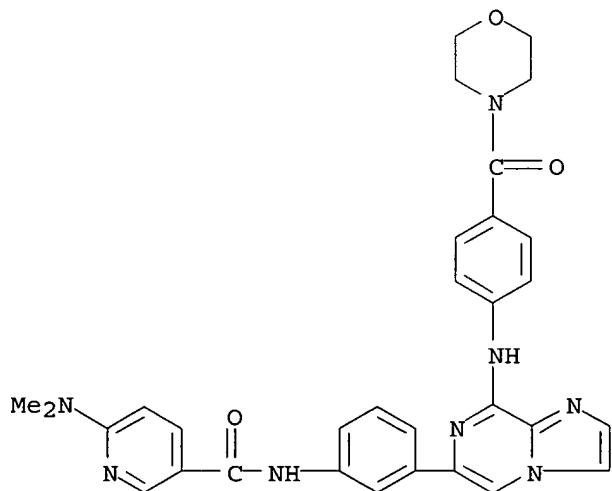
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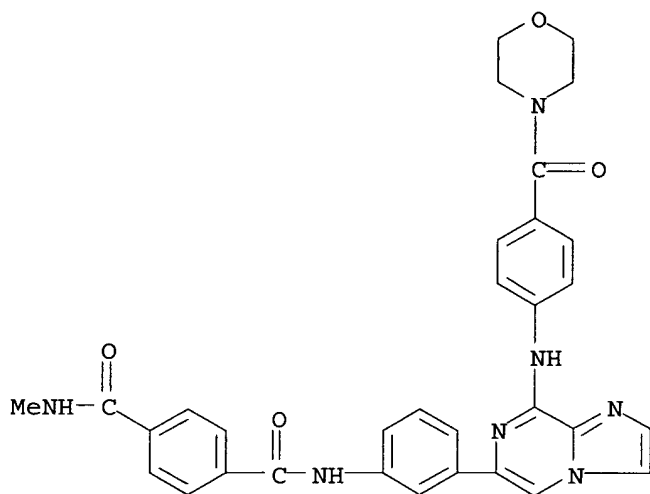
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(CA INDEX NAME)



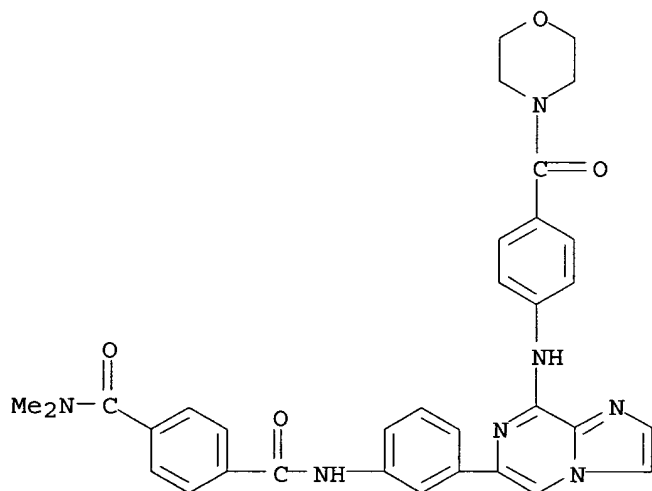
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CN 1,4-Benzenedicarboxamide, N-methyl-N'-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



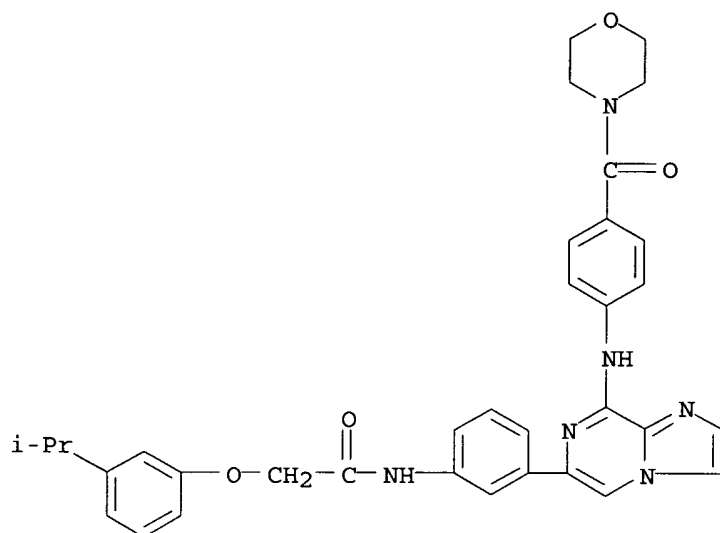
RN 845271-26-3 HCAPLUS

CN 1,4-Benzenedicarboxamide, N,N-dimethyl-N'-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI)
(CA INDEX NAME)

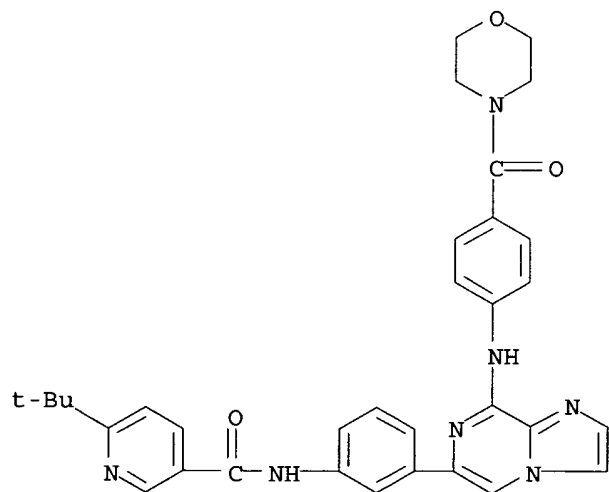


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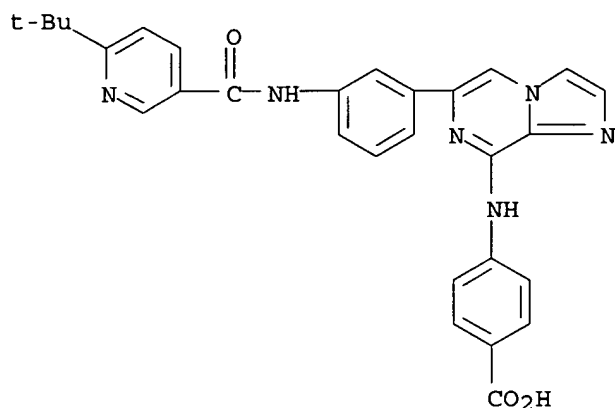
CN Benzamide, 4-acetyl-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



| | | |
|----|--|---------|
| RN | 845271-32-1 | HCAPLUS |
| CN | 3-Pyridinecarboxamide, 6-(1,1-dimethylethyl)-N-[3-[8-[[4-(4-morpholinylcarbonyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) | |
| | (CA INDEX NAME) | |



RN 845271-34-3 HCAPLUS
CN Benzoic acid, 4-[[[6-[3-[[[6-(1,1-dimethylethyl)-3-pyridinyl]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:58205 HCAPLUS

DOCUMENT NUMBER: 142:155976

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as Bruton's tyrosine kinase (Btk) inhibitors for the treatment of cancer

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Mitchell, Scott; Pippin, Douglas A.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|--|------------|
| WO 2005005429 | A1 | 20050120 | WO 2004-US21150 | 20040630 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005101604 | A1 | 20050512 | US 2004-883646 | 20040630 |
| PRIORITY APPLN. INFO.: | | | US 2003-484014P | P 20030630 |
| OTHER SOURCE(S): | | | CASREACT 142:155976; MARPAT 142:155976 | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = -Z2-Q-R2; Z2 = divalent linking group, i.e., para-phenylene, meta-phenylene, ortho-phenylene, etc.; Q = CON(R4), N(R4)CO; R1 = (un)substituted indole, indazole, benzoxazole, etc.; R2 = alkyl, cycloalkyl, heterocycloalkyl, etc.; R3 = H, alkyl, heterocycloalkyl, etc.; R4 = H, alkyl, (un)substituted Ph etc.] and their pharmaceutically acceptable salts were prepared For example, p-tert-Bu benzoyl chloride acylation of aniline II, i.e., prepared from 3,5-dibromo-2-aminopyrazine in 3-steps, afforded claimed imidazopyrazinylamine III. Compds. I are claimed to be useful for the treatment of cancer, autoimmune and/or inflammatory disease or acute inflammatory reaction.

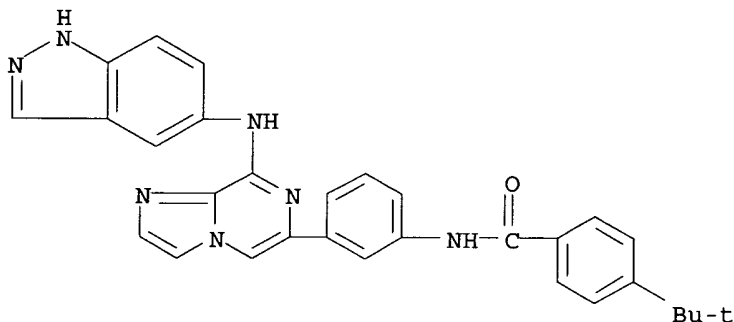
IT **828300-64-7P**, 4-tert-Butyl-N-[3-[8-(1H-indazol-5-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **828300-65-8P**
828300-66-9P **828300-67-0P** **828300-68-1P**
828300-69-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazo[1,2-a]pyrazinylamines as Bruton's tyrosine kinase (Btk) inhibitors for the treatment of cancer)

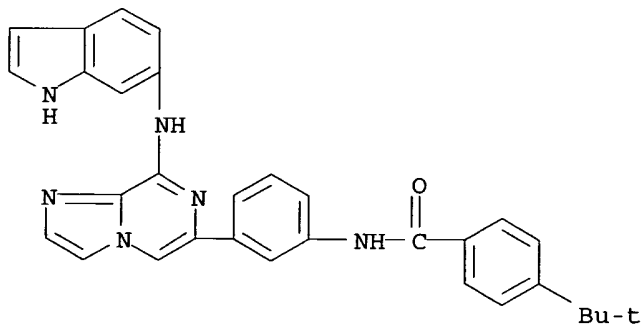
RN 828300-64-7 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-(1H-indazol-5-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



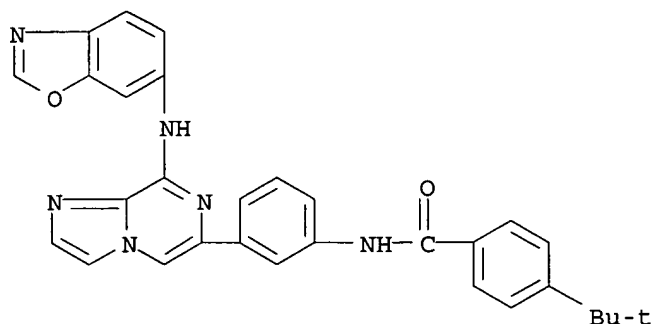
RN 828300-65-8 HCAPLUS

CN Benzamide, 4-(1,1-dimethylethyl)-N-[3-[8-(1H-indol-6-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



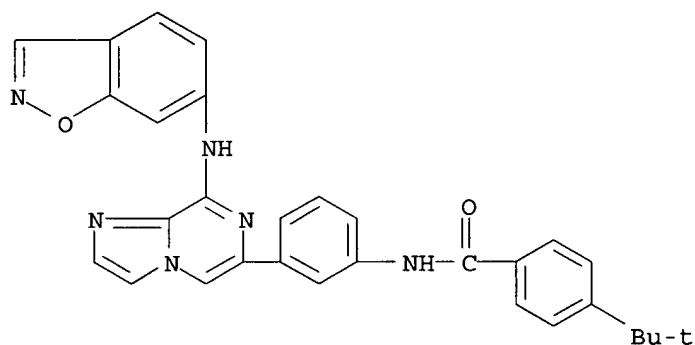
RN 828300-66-9 HCAPLUS

CN Benzamide, N-[3-[8-(6-benzoxazolylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



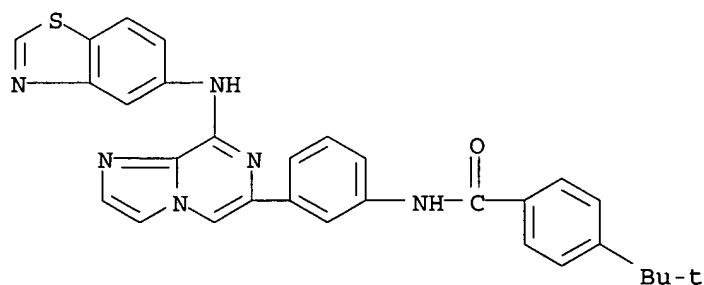
RN 828300-67-0 HCAPLUS

CN Benzamide, N-[3-[8-(1,2-benzisoxazol-6-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



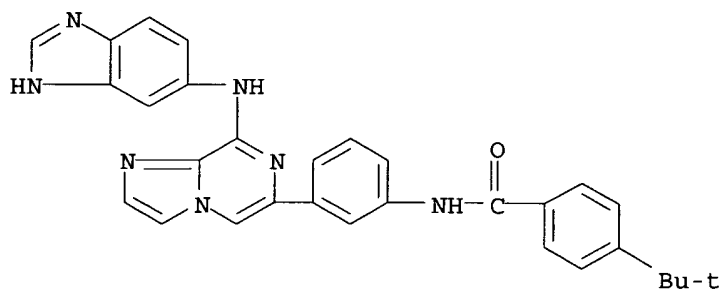
RN 828300-68-1 HCAPLUS

CN Benzamide, N-[3-[8-(5-benzothiazolylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 828300-69-2 HCAPLUS

CN Benzamide, N-[3-[8-(1H-benzimidazol-5-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-4-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:34601 HCAPLUS

DOCUMENT NUMBER: 142:134621

TITLE: Preparation of aryl-substituted 8-aminoarylimidazo[1,2-a]pyrazines as kinase inhibitors for treatment of cancer and other conditions

INVENTOR(S): Sun, Connie Li; Liang, Congxin; Huang, Ping; Harris, G. Davis; Guan, Huiping

PATENT ASSIGNEE(S): Sugan, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 119 pp., Cont.-in-part of U.S. Ser. No. 781,928.

CODEN: USXXCO

DOCUMENT TYPE: Patent

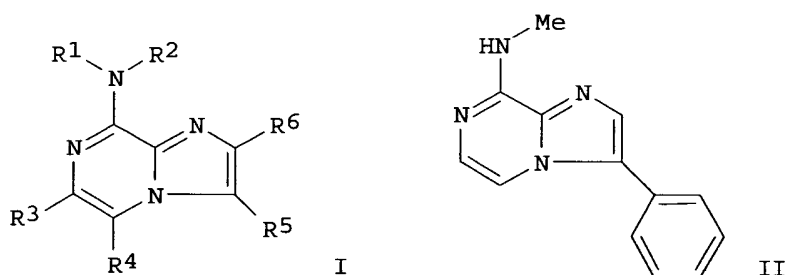
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2005009832 | A1 | 20050113 | US 2004-845586 | 20040514 |
| US 2004220189 | A1 | 20041104 | US 2004-781928 | 20040220 |
| PRIORITY APPLN. INFO.: | | | US 2003-448114P | P 20030220 |
| | | | US 2003-508860P | P 20031007 |
| | | | US 2004-781928 | A2 20040220 |

OTHER SOURCE(S): MARPAT 142:134621
GI



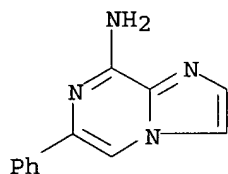
AB The title compds. I [wherein R1, R2 = H, (cyclo)alkyl, (hetero)aryl, etc.; R3, R4 = H, halo, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.; R5 = H, halo, (un)substituted (hetero)aryl; wherein at least one of R4 and R5 =

(hetero)aryl; R6 = H; or pharmaceutically acceptable salts and prodrugs thereof] were prepared as protein kinase (PK) inhibitors. For example, amination of 3,5-dibromoimidazo[1,2-a]pyrazine with methylamine in THF afforded (3-bromoimidazo[1,2-a]pyrazin-8-yl)methylamine (50%), which was coupled with phenylboronic acid in THF to give II (63%). Various assays which may be used to determine the level of activity of compds. I against one or more PKs (such as GST-Flk1 receptor tyrosine kinase, fibroblast growth factor type 1 receptors (FGFR1), and platelet-derived growth factor (PDGF) receptors) were described in detail (no data given). Thus, I and pharmaceutical compns. comprising these compds. are useful for treating disorders related to abnormal PK activity, such as cancer, diabetes, autoimmune disorders, inflammatory disorders, and cardiovascular disorders (no data).

IT 673857-28-8P, (6-Phenylimidazo[1,2-a]pyrazin-8-yl)amine
 787591-86-0P, Methyl(6-phenylimidazo[1,2-a]pyrazin-8-yl)amine
 787591-87-1P, 4-(8-Methylaminoimidazo[1,2-a]pyrazin-6-yl)phenol
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (kinase inhibitor; preparation of imidazo[1,2-a]pyrazines as kinase inhibitors for treatment of cancer and other conditions)

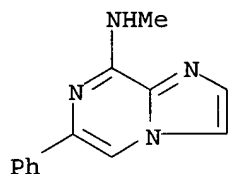
RN 673857-28-8 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl- (9CI) (CA INDEX NAME)



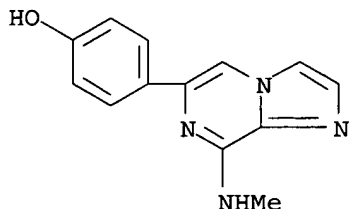
RN 787591-86-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-methyl-6-phenyl- (9CI) (CA INDEX NAME)



RN 787591-87-1 HCAPLUS

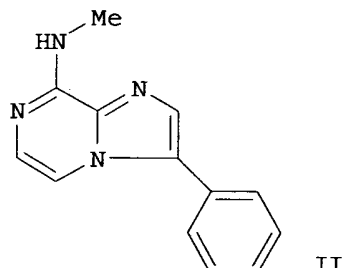
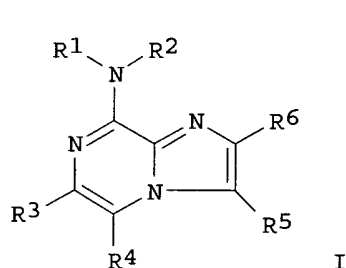
CN Phenol, 4-[8-(methylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:934327 HCAPLUS
 DOCUMENT NUMBER: 141:395578
 TITLE: Preparation of aryl-substituted 8-aminoarylimidazo[1,2-
 a]pyrazines as kinase inhibitors for treatment of
 cancer and other conditions
 INVENTOR(S): Sun, Connie Li; Liang, Congxin; Huang, Ping; Harris,
 G. Davis; Guan, Huiping
 PATENT ASSIGNEE(S): Sugan, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 76 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004220189 | A1 | 20041104 | US 2004-781928 | 20040220 |
| US 2005009832 | A1 | 20050113 | US 2004-845586 | 20040514 |
| PRIORITY APPLN. INFO.: | | | US 2003-448114P | P 20030220 |
| | | | US 2003-508860P | P 20031007 |
| | | | US 2004-781928 | A2 20040220 |

OTHER SOURCE(S): MARPAT 141:395578
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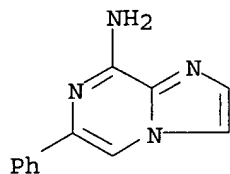
- AB Title compds. I [wherein R1, R2 = independently H, acyl, carbamoyl, alkoxy, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.; R3, R4 = independently H, halo, OH, acyl, carbamoyl, alkoxy, sulfamoyl, CN, NO2, NH2, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.; R5 = H, halo, (un)substituted aryl; wherein at least one of R3, R4, and R5 = aryl; R6 = H; or pharmaceutically acceptable salts and prodrugs thereof] were prepared as protein kinase (PK) inhibitors. For example, amination of 3,5-dibromoimidazo[1,2-a]pyrazine with methylamine in THF afforded (3-bromoimidazo[1,2-a]pyrazin-8-yl)methylamine (50%), which was coupled with phenylboronic acid in THF to give II (63%). Nine exemplified compds. were tested and found active against GST-Flk1 receptor tyrosine kinase, fibroblast growth factor type 1 receptors (FGFR1), and platelet-derived growth factor (PDGF) receptors (no data). Thus, I and pharmaceutical compns. comprising these compds. are useful for treating disorders related to abnormal PK activity, such as cancer, diabetes, autoimmune disorders, inflammatory disorders, and cardiovascular disorders (no data).
- IT 673857-28-8P, (6-Phenylimidazo[1,2-a]pyrazin-8-yl)amine
 787591-86-0P, Methyl(6-phenylimidazo[1,2-a]pyrazin-8-yl)amine
 787591-87-1P, 4-(8-Methylaminoimidazo[1,2-a]pyrazin-6-yl)phenol

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(kinase inhibitor; preparation of imidazo[1,2-a]pyrazines as kinase inhibitors for treatment of cancer and other conditions)

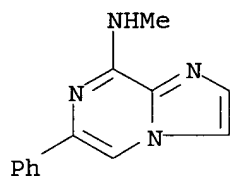
RN 673857-28-8 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl- (9CI) (CA INDEX NAME)



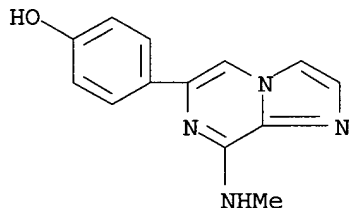
RN 787591-86-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-methyl-6-phenyl- (9CI) (CA INDEX NAME)



RN 787591-87-1 HCAPLUS

CN Phenol, 4-[8-(methylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:696382 HCAPLUS

DOCUMENT NUMBER: 141:225538

TITLE: Certain 8-heteroaryl-6-phenyl-imidazo[1,2-a]pyrazines as modulators of kinase activity, particularly EphB4 kinase, and their preparation, pharmaceutical compositions, and methods of use for modulation and treatment of diseases and disorders

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

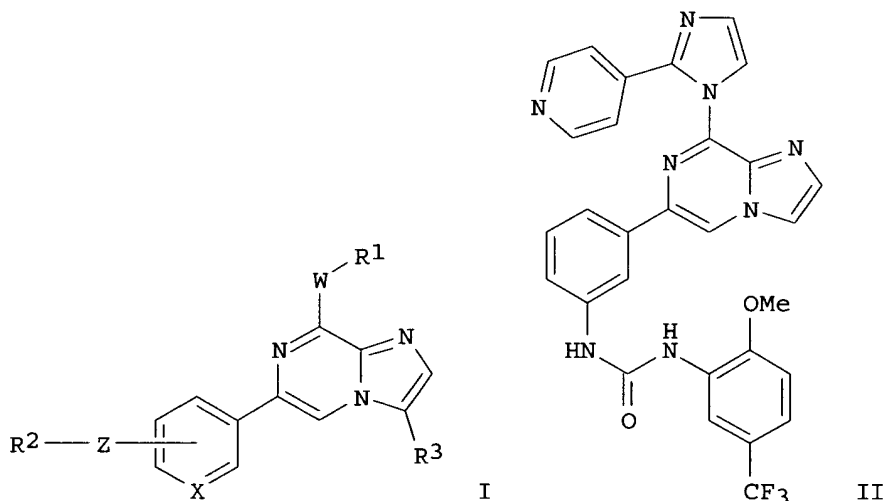
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2004072081 | A1 | 20040826 | WO 2004-US3923 | 20040210 |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MZ, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005054648 | A1 | 20050310 | US 2004-776002 | 20040210 |
| US 2005054649 | A1 | 20050310 | US 2004-776631 | 20040210 |
| PRIORITY APPLN. INFO.: | | | US 2003-446379P | P 20030210 |
| OTHER SOURCE(S): | | MARPAT 141:225538 | | |

GI



AB The invention pertains to compds. I and all pharmaceutically acceptable forms thereof [wherein: R1 = pyridyl or pyrimidinyl (un)substituted with 0-3 selected substituents; W = Ph or 5- or 6-membered N/O/S heteroaryl with 1-4 heteroatoms and 0-3 selected substituents; X = N or CH; R2 = (alkoxy)alkyl, (hetero)cycloalkyl(alkyl), (alkoxy)alkoxy; or R2 = phenyl(alkyl) or heteroaryl(alkyl) bearing 0-3 selected substituents; Z = (CR8R9)_n, CONR10, NR10CO, or NR10CONR11; R8, R9 = H, alkyl, alkoxy, halo; n = 0-2; R10, R11 = H, alkyl, or Ph or heteroaryl with 0-3 selected substituents; R3 = H, alkyl; or R3 = (hetero)cycloalkyl(alkyl), Ph, or heteroaryl each bearing 0-3 selected substituents; or R3 = phenoxyphenyl with each ring bearing 0-3 selected substituents]. Addnl. compds. with a linker group between R1 and W are disclosed but neither claimed nor prepared

The compds. are modulators of kinase activity and Hsp90 complex activity. In particular, they are highly active inhibitors of angiogenic and oncogenic kinases. The invention also provides pharmaceutical compns. containing one or more compound I, or a pharmaceutically acceptable form of

such

compds., and one or more pharmaceutically acceptable carriers, excipients, or diluents. The invention further comprises methods of treating patients suffering from certain diseases and disorders responsive to EphB4 kinase modulation, which comprise administering to such patients an amount of a compound I effective to reduce signs or symptoms of the disease or disorder. These diseases include cancer, including breast neoplasms, endometrial cancer, colon cancer, and neck squamous cell carcinoma. The methods of treatment include administering a sufficient amount of I or a salt to decrease the symptoms or slow the progression of these diseases or disorders. The invention also encompasses methods of treating other animals, including livestock and domesticated companion animals, suffering from a disease or disorder responsive to EphB4 modulation. Methods of treatment include administering I as a single active agent or administering a compound I in combination with one or more other therapeutic agents. The invention also includes a method for determining the presence of EphB4 kinase in a sample, comprising contacting the sample with a compound I, or form thereof, and detecting the amount of compound or form bound to EphB4 kinase, and therefrom determining the presence or absence of EphB4 kinase in the sample. Ten compds. I were prepared in examples. For instance, compound II was prepared in 4 steps: (1) deprotection of BrCH₂CH(OMe)₂ with HBr and cyclocondensation with 3,5-dibromo-2-aminopyrazine to give 6,8-dibromoimidazo[1,2-a]pyrazine; (2) aminolysis of the 8-bromo with 4-(1H-imidazol-2-yl)pyridine; (3) Suzuki coupling of the 6-bromo with 3-H₂NC₆H₄B(OH)₂.HCl; and (4) carbamoylation of the amino group with 2-isocyanato-1-methoxy-4-(trifluoromethyl)benzene. In an assay for EphB4 kinase activity, using human recombinant EphB4 kinase cytoplasmic domain (Genbank Accession Number AY056047), compds. I had IC₅₀ values of 10 μM or less, with some particularly preferred compds. having values of 100 nM or less. Similar inhibitory potencies were found against VEGF-R2, c-Kit, and Tie-2 kinases in vitro.

IT

746642-12-6P, 1-(2-Methoxy-5-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-13-7P, 1-(4-Methoxy-3-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-14-8P, 1-(2-Methoxy-5-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-3-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-15-9P, 1-(5-Chloro-2-methoxyphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-16-0P, 1-(5-Fluoro-2-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-17-1P, 1-(5-Chloro-2-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-18-2P, 1-[5-Chloro-2,4-di(methyloxy)phenyl]-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-19-3P, 1-(4-Methyl-3-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

746642-20-6P, 1-(4-Chloro-3-trifluoromethylphenyl)-3-[3-[8-[2-(pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

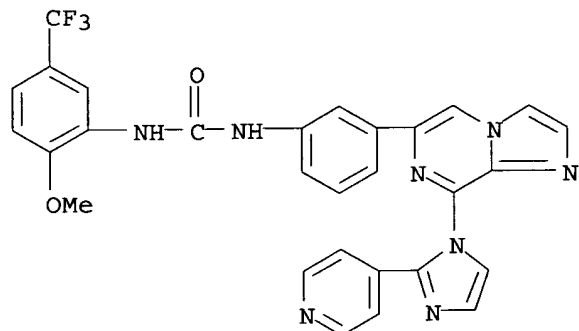
746642-21-7P, 1-(2-Methoxy-5-trifluoromethylphenyl)-3-[3-[8-[3-(pyridin-4-yl)pyrazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of heteroarylphenylimidazopyrazines as kinase modulators for treatment of cancer and angiogenesis)

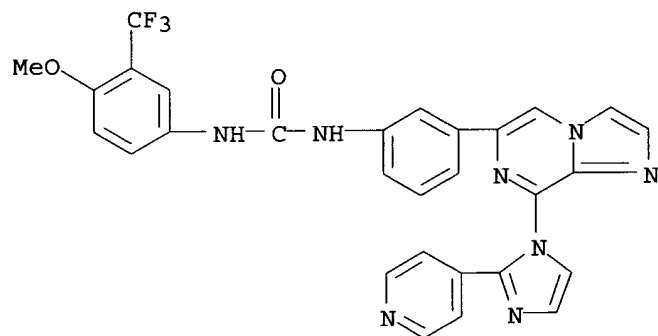
RN 746642-12-6 HCAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



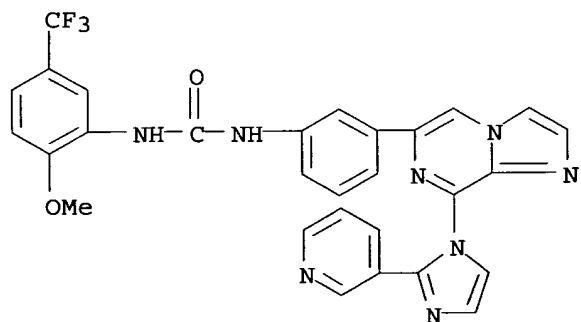
RN 746642-13-7 HCAPLUS

CN Urea, N-[4-methoxy-3-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



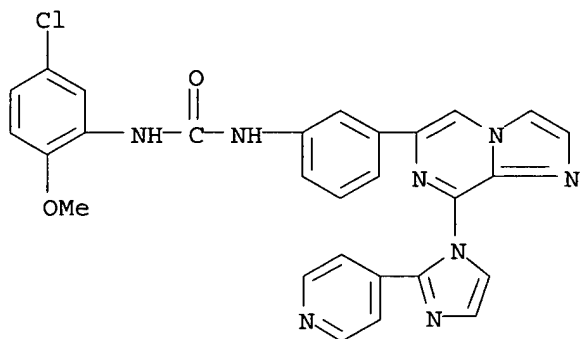
RN 746642-14-8 HCAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(3-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



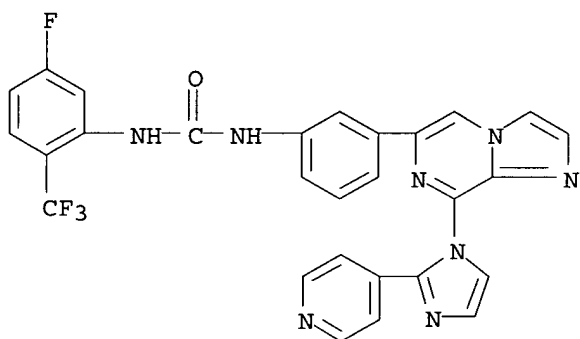
RN 746642-15-9 HCAPLUS

CN Urea, N-(5-chloro-2-methoxyphenyl)-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



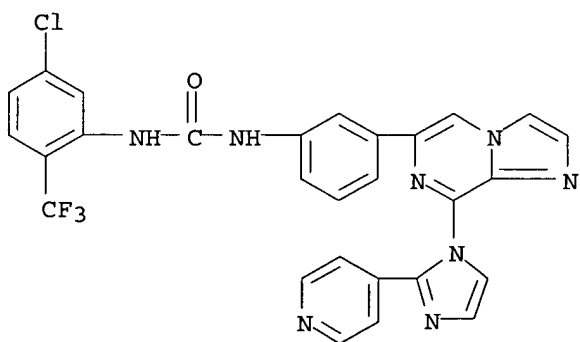
RN 746642-16-0 HCAPLUS

CN Urea, N-[5-fluoro-2-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



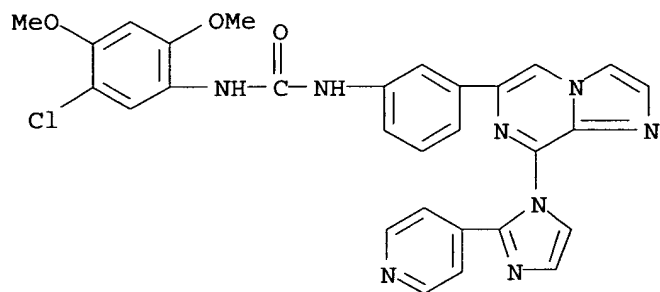
RN 746642-17-1 HCAPLUS

CN Urea, N-[5-chloro-2-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



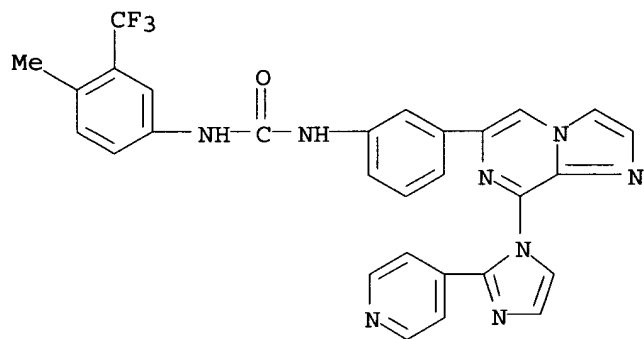
RN 746642-18-2 HCAPLUS

CN Urea, N-(5-chloro-2,4-dimethoxyphenyl)-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



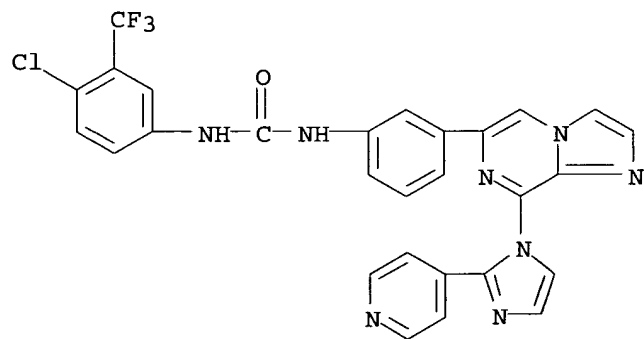
RN 746642-19-3 HCAPLUS

CN Urea, N-[4-methyl-3-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



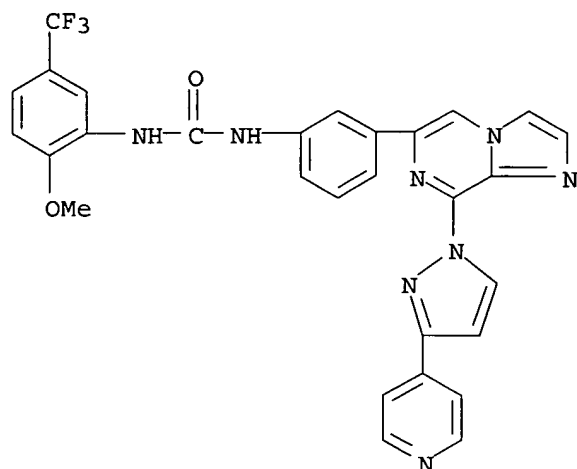
RN 746642-20-6 HCAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

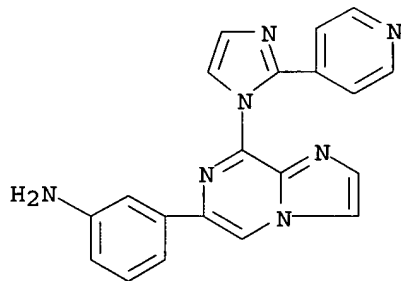


RN 746642-21-7 HCAPLUS

CN Urea, N-[2-methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[8-[3-(4-pyridinyl)-1H-pyrazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

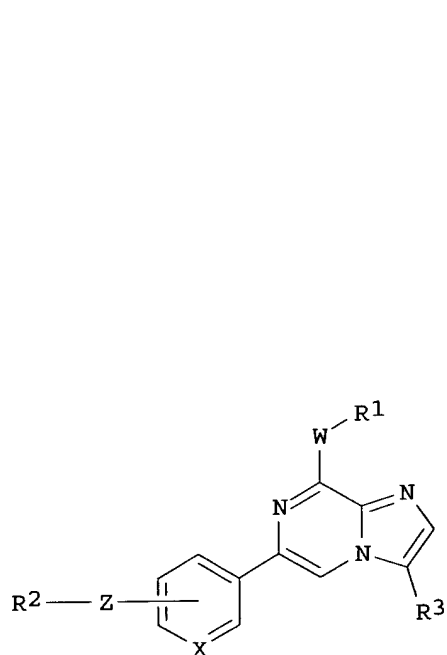


IT 746642-23-9P, 3-[8-[2-(Pyridin-4-yl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenylamine
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of heteroarylphenylimidazopyrazines as kinase modulators for treatment of cancer and angiogenesis)
 RN 746642-23-9 HCAPLUS
 CN Benzenamine, 3-[8-[2-(4-pyridinyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)

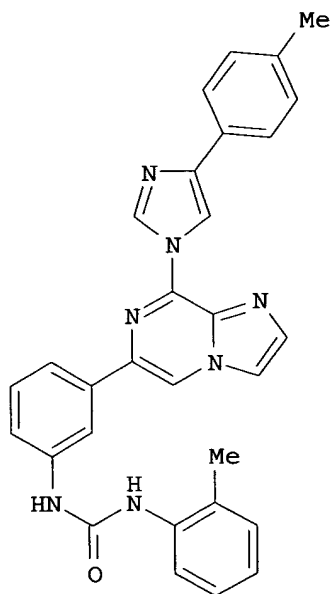


L4 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:696381 HCAPLUS
 DOCUMENT NUMBER: 141:225537
 TITLE: Certain 8-heteroaryl-6-phenyl-imidazo[1,2-a]pyrazines as modulators of Hsp90 complex activity and their preparation, pharmaceutical compositions, and methods of use
 INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.
 PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA
 SOURCE: PCT Int. Appl., 106 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2004072080 | A1 | 20040826 | WO 2004-US3922 | 20040210 |
| W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, LC, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005054648 | A1 | 20050310 | US 2004-776002 | 20040210 |
| US 2005054649 | A1 | 20050310 | US 2004-776631 | 20040210 |
| PRIORITY APPLN. INFO.: | | | US 2003-446379P | P 20030210 |
| OTHER SOURCE(S): | | MARPAT 141:225537 | | |
| GI | | | | |



I



II

AB The invention pertains to compds. I and all pharmaceutically acceptable forms thereof [wherein: R¹ = H, halo, alkyl, alkoxy, (hetero)cycloalkyl(alkyl), sulfonamide, alkoxyalkyl, alkoxyalkoxy, (di)alkylamino(alkyl); or R¹ = Ph or a benzo-fused 5- to 7-membered N/O/S heterocycloalkyl bearing 0-3 selected substituents; W = Ph or 5- or 6-membered N/O/S heteroaryl with 1-4 heteroatoms and 0-3 selected substituents; X = N or CH; R² = (alkoxy)alkyl, (hetero)cycloalkyl(alkyl), (alkoxy)alkoxy; or R² = phenyl(alkyl) or heteroaryl(alkyl) bearing 0-3 selected substituents; Z = (CR⁸R⁹)_n, CONR¹⁰, NR¹⁰CO, or NR¹⁰CONR¹¹; R⁸, R⁹

= H, alkyl, alkoxy, halo; n = 0-2; R10, R11 = H, alkyl, or Ph or heteroaryl with 0-3 selected substituents; R3 = H, alkyl; or R3 = (hetero)cycloalkyl(alkyl), Ph, or heteroaryl each bearing 0-3 selected substituents; or R3 = phenoxyphenyl with each ring bearing 0-3 selected substituents]. Addnl. compds. with a linking group between R1 and W are disclosed but neither prepared nor claimed. The compds. I are modulators of kinase activity and Hsp90 complex activity. Certain compds. I are highly active inhibitors of Hsp90 complex activity. The invention also provides pharmaceutical compns. containing one or more compound I, or a pharmaceutically acceptable form of such compds., and one or more pharmaceutically acceptable carriers, excipients, or diluents. The invention further comprises methods of treating patients suffering from certain diseases and disorders responsive to Hsp90 complex modulation, which comprise administering to such patients an amount of a compound I effective to reduce signs or symptoms of the disease or disorder. These diseases include cancer, including chronic myeloid leukemia, melanoma, breast, ovarian, brain, thyroid, colorectal, prostate, and bladder cancer, heart disease, stroke, autoimmune/inflammatory diseases, and neurodegenerative diseases. The methods of treatment include administering a sufficient amount of a compound I or a form thereof to decrease the symptoms or slow the progression of these diseases or disorders. The invention also encompasses methods of treating non-human patients, including livestock and domesticated companion animals, suffering from a disease or disorder responsive to Hsp90 complex modulation. Methods of treatment include administering a compound I as a single active agent or administering a compound I in combination with one or more other therapeutic agents. The invention also includes a method for determining the presence of certain

kinases

or Hsp90 complex in a sample, comprising contacting the sample with a compound I, or form thereof, and detecting Hsp90 complex activity in the sample. Almost 50 compds. I were prepared in examples. For instance, compound II was prepared in 4 steps: (1) deprotection of BrCH₂CH(OEt)₂ with HBr and cyclocondensation with 3,5-dibromo-2-aminopyrazine to give 6,8-dibromimidazo[1,2-a]pyrazine; (2) aminolysis of the 8-bromo with 4-(p-tolyl)-1H-imidazole; (3) Suzuki coupling of the 6-bromo with 3-H₂NC₆H₄B(OH)₂.HCl; and (4) carbamoylation of the amino group with 1-isocyanato-2-methylbenzene. In a tumor cell monolayer proliferation assay using MCF-7 or HCT-15 cells, compds. I had IC₅₀ values of 25 μM or less, with certain compds. having values of 10 μM or less.

IT **746653-81-6P**, 1-[3-[8-(4-Phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **746653-82-7P**, 1-(4-Chlorophenyl)-3-[3-[8-(4-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-83-8P**, 1-(2-Methylsulfonylphenyl)-3-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-84-9P**, 1-[3-[8-(2-Phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **746653-85-0P**, 1-(4-Chlorophenyl)-3-[3-[8-[4-(4-chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-86-1P**, 1-[3-[8-[4-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **746653-87-2P**, 1-(4-Chlorophenyl)-3-[3-[8-(4-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-88-3P**, 1-o-Tolyl-3-[3-[8-(4-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-89-4P**, 1-(4-Chlorophenyl)-3-[3-[8-(4-methylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-90-7P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[4-(4-chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-91-8P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(4-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-92-9P**, 1-[3-[8-[4-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[4-[(4-methylpiperazin-1-yl)methyl]phenyl]urea **746653-93-0P**,

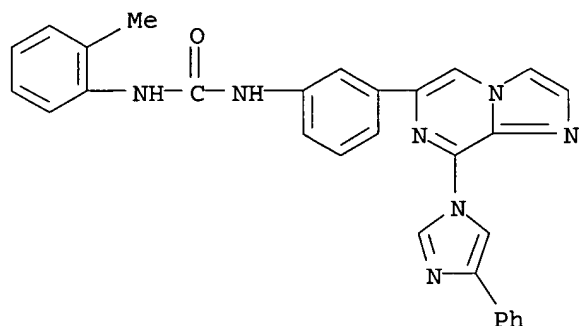
1-[3-[8-[4-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[4-[(morpholin-4-yl)methyl]phenyl]urea **746653-94-1P**,
 1-[3-[8-[4-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[4-[[3-ethoxypropyl]amino]methyl]phenyl]urea **746653-95-2P**,
 1-(4-Chlorophenyl)-3-[3-[8-(3-phenylpyrazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-96-3P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(3-phenylpyrazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-97-4P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746653-98-5P**,
 4-Chloro-N-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746653-99-6P**,
 3-[(Morpholin-4-yl)methyl]-N-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-00-2P**,
 4-[(Morpholin-4-yl)methyl]-N-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-01-3P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-02-4P**,
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 6-[4-[(Morpholin-4-yl)methyl]phenyl]-8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazine **746654-05-7P**,
 1-(4-Chlorophenyl)-3-[3-[8-(2-o-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-06-8P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-o-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-07-9P**,
 1-(4-Chlorophenyl)-3-[3-[8-[2-(2-methoxyphenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-08-0P**,
 1-(4-Chlorophenyl)-3-[3-[8-[2-(2-fluorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-09-1P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[2-(2-fluorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-10-4P**,
 1-[3-[8-[2-(2-Fluorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **746654-11-5P**,
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 1-(4-Chlorophenyl)-3-[3-[8-(2-isopropylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-13-7P**,
 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-isopropylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **746654-14-8P**,
 1-[3-[8-(4-Bromoimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **746654-15-9P**,
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 2,6-Dimethyl-N-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-20-6P**,
 4-Fluoro-N-[3-[8-(2-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-21-7P**,
 3-Methoxy-N-[3-[8-(2-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-22-8P**,
 3-Methoxy-4-methyl-N-[3-[8-(2-p-tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **746654-23-9P**,
 2-(4-Chlorophenyl)-N-[3-[8-(2-phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]acetamide **746654-24-0P**,
 2-(4-Chlorophenyl)-N-[3-[8-[2-(4-chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]acetamide **746654-25-1P**,
 N-[3-[8-[2-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-2-(3-trifluoromethylphenyl)acetamide **746654-26-2P**,
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a]pyrazin-6-yl]phenyl]-3-[4-[(morpholin-4-yl)methyl]phenyl]urea
746654-27-3P, 1-(4-Chlorobenzyl)-3-[3-[8-[2-(4-chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea
746654-28-4P, 1-[3-[8-[2-(4-Chlorophenyl)imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[4-(4-methylpiperazin-1-ylmethyl)phenyl]urea
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of heteroarylphenylimidazopyrazines as modulators of Hsp90 complex activity)

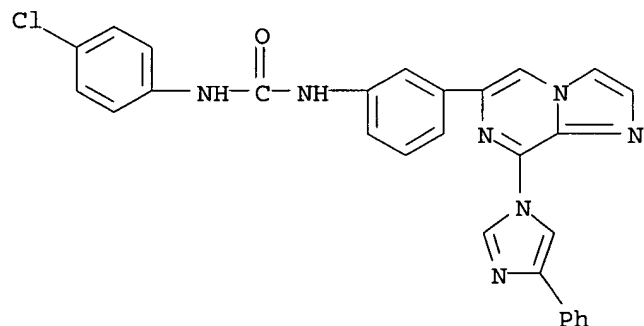
RN 746653-81-6 HCAPLUS

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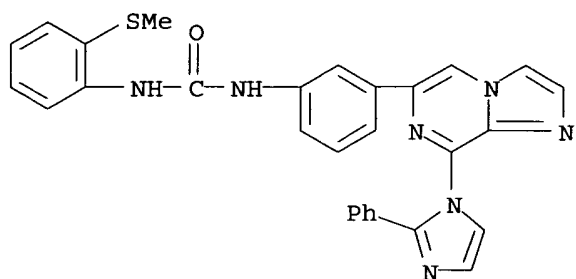
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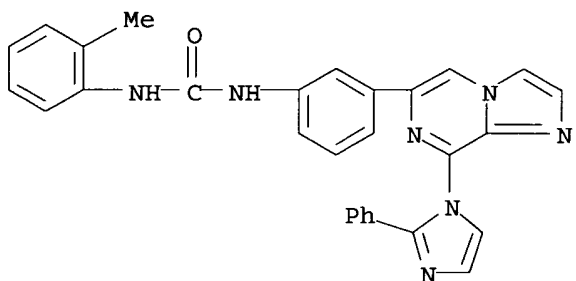
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CN Urea, N-[2-(methylthio)phenyl]-N'-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



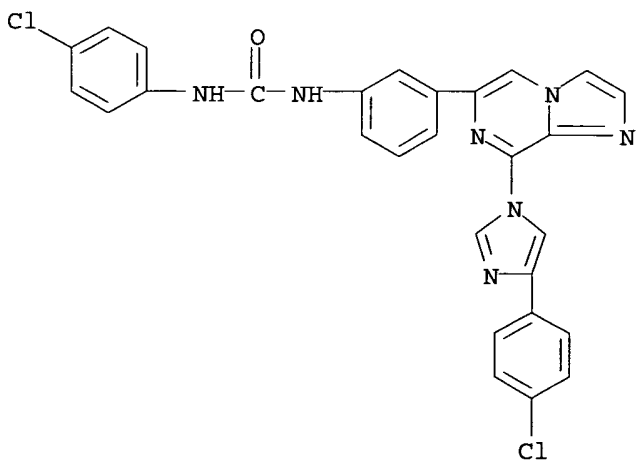
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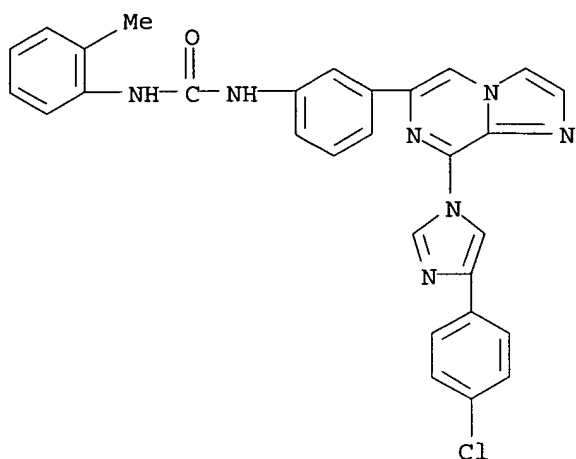
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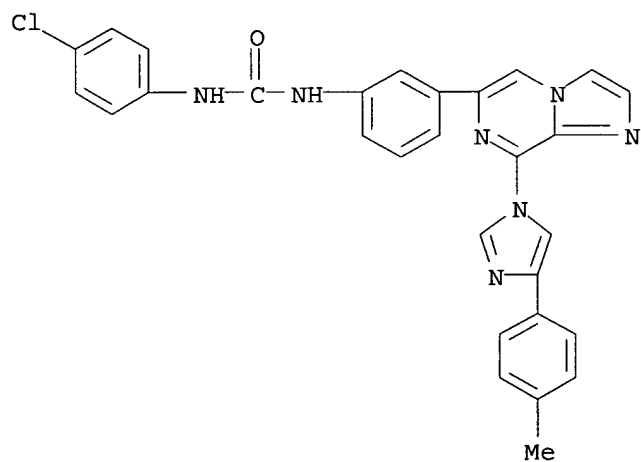


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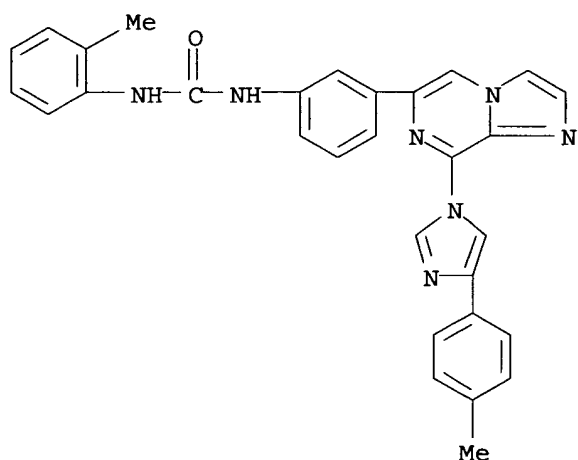
CN Urea, N-[3-[8-[4-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 746653-87-2 HCAPLUS
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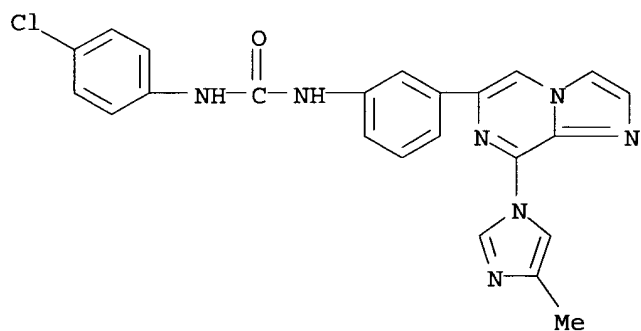


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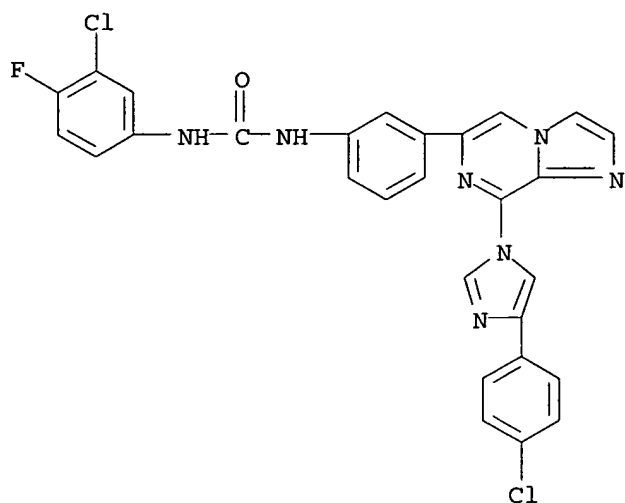
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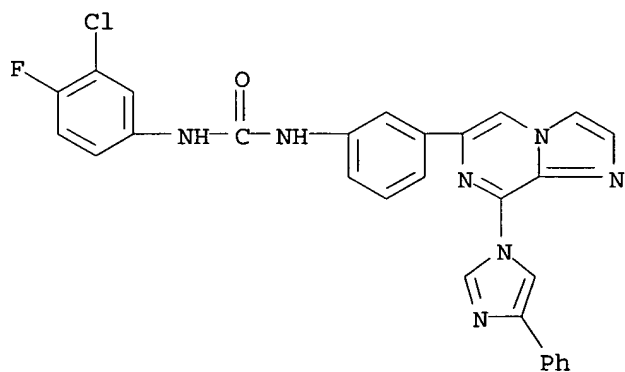
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RN 746653-91-8 HCAPLUS

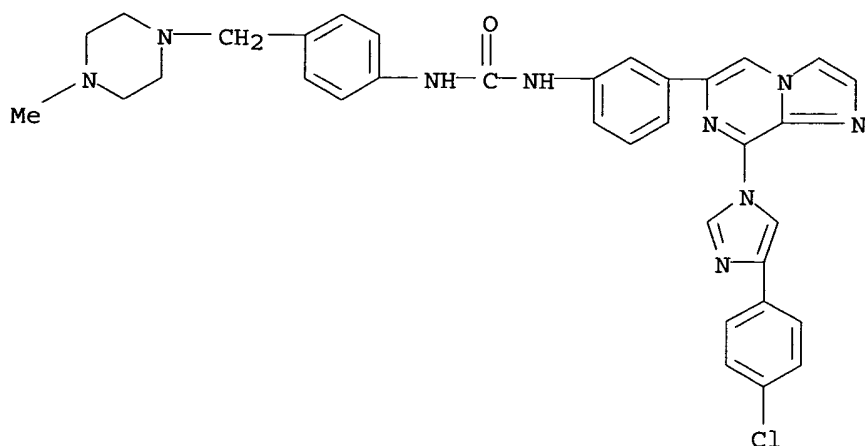
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RN 746653-92-9 HCAPLUS

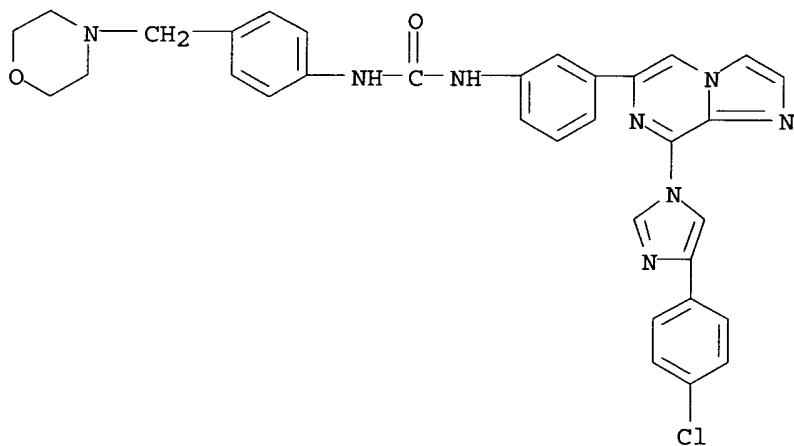
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Ward 10_658121



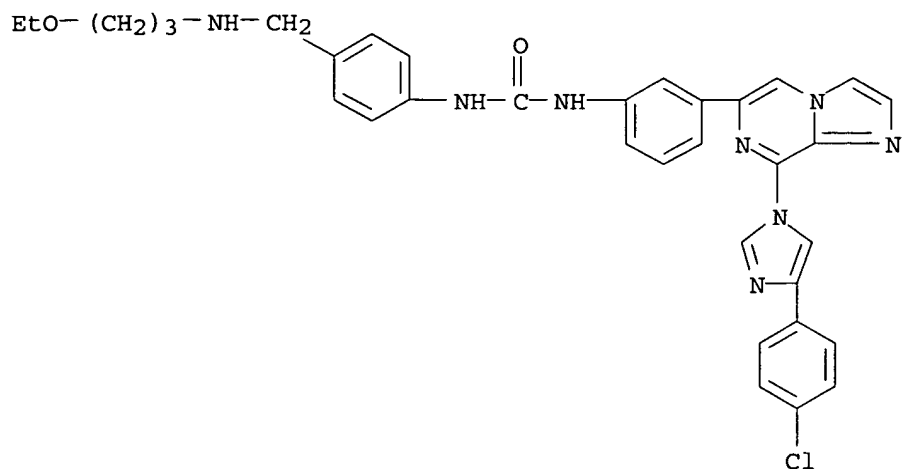
RN 746653-93-0 HCAPLUS

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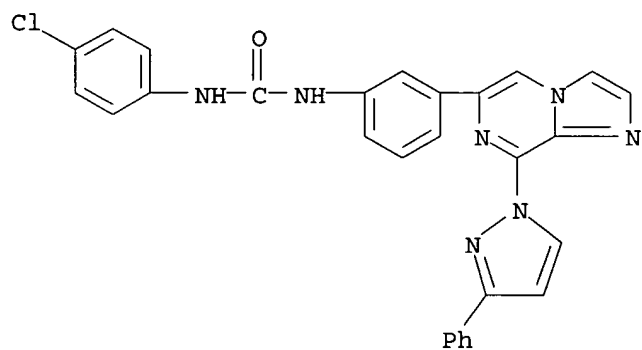
RN 746653-94-1 HCAPLUS

CN Urea, N-[3-[8-[4-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-[(3-ethoxypropyl)amino]methyl]phenyl]- (9CI) (CA INDEX NAME)



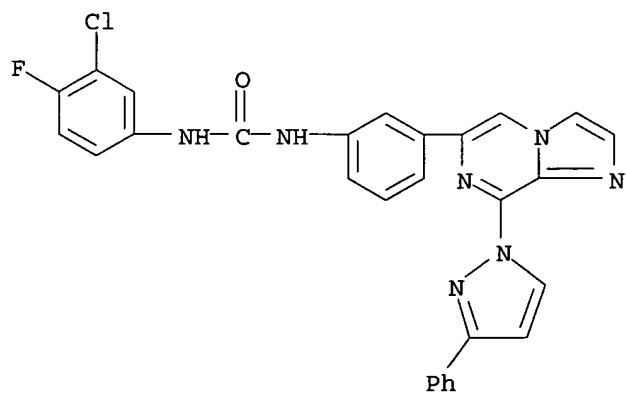
RN 746653-95-2 HCAPLUS

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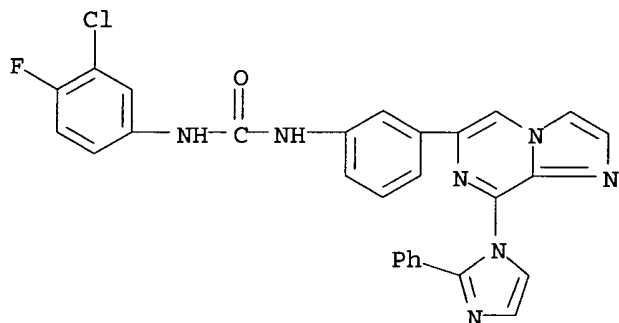
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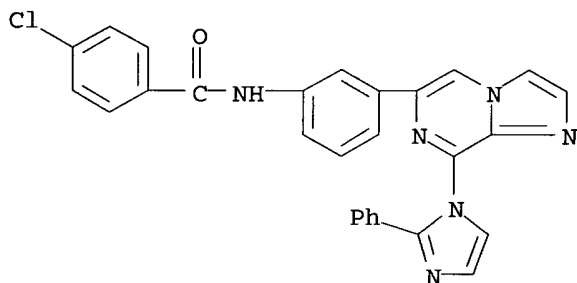
RN 746653-97-4 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



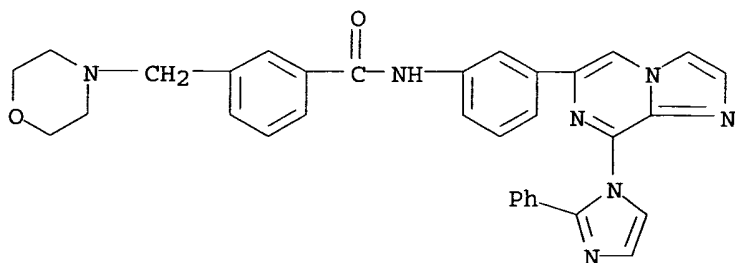
RN 746653-98-5 HCAPLUS

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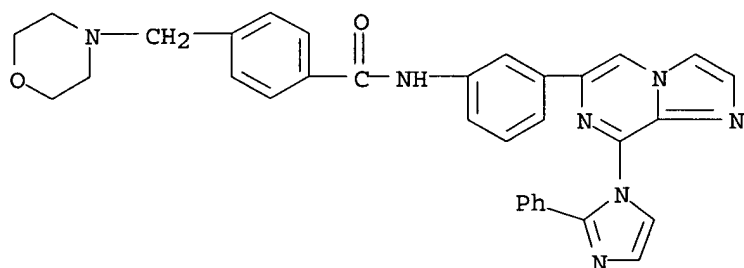
RN 746653-99-6 HCAPLUS

CN Benzamide, 3-(4-morpholinylmethyl)-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



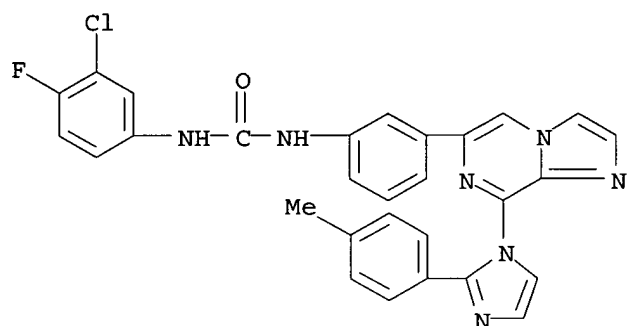
RN 746654-00-2 HCAPLUS

CN Benzamide, 4-(4-morpholinylmethyl)-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



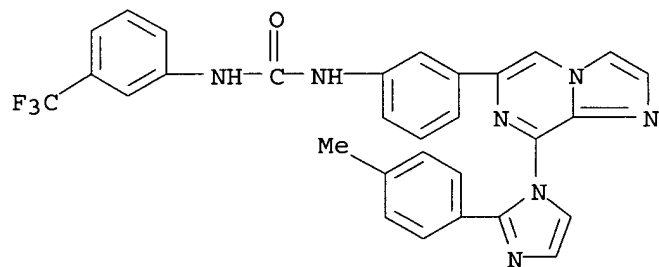
RN 746654-01-3 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[2-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



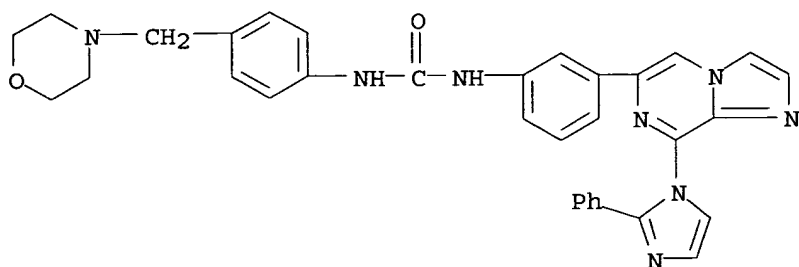
RN 746654-02-4 HCAPLUS

CN Urea, N-[3-[8-[2-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

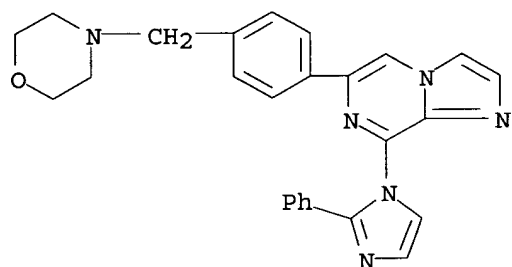


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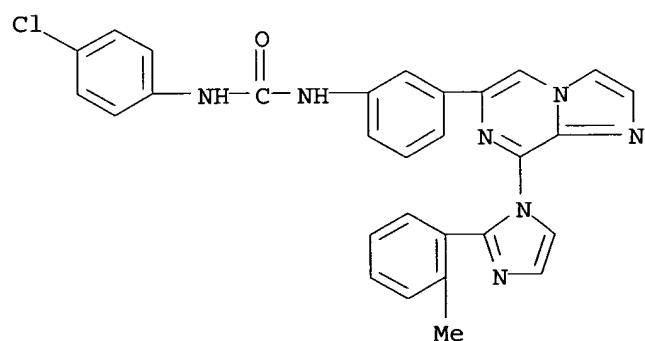
CN Urea, N-[4-(4-morpholinylmethyl)phenyl]-N'-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



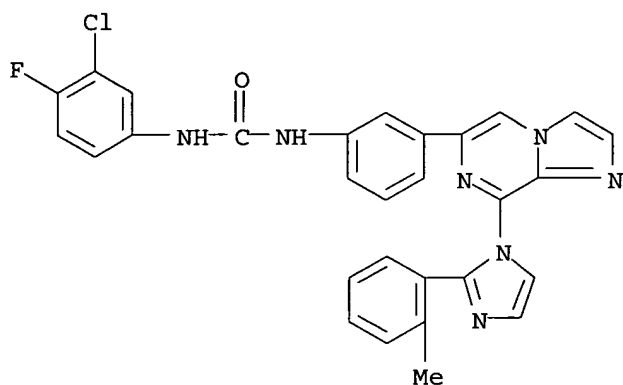
RN 746654-04-6 HCAPLUS
 CN Imidazo[1,2-a]pyrazine, 6-[4-(4-morpholinylmethyl)phenyl]-8-(2-phenyl-1H-imidazol-1-yl)- (9CI) (CA INDEX NAME)



RN 746654-05-7 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[2-(2-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

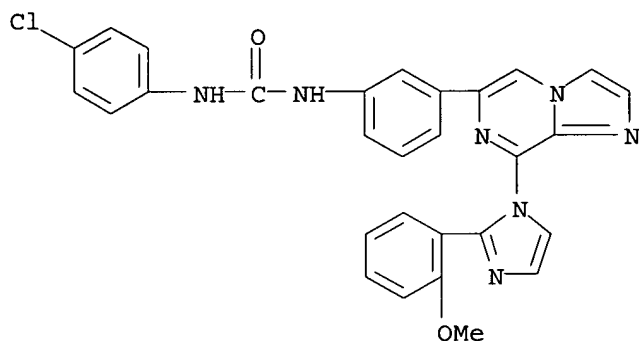


RN 746654-06-8 HCAPLUS
 CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[2-(2-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



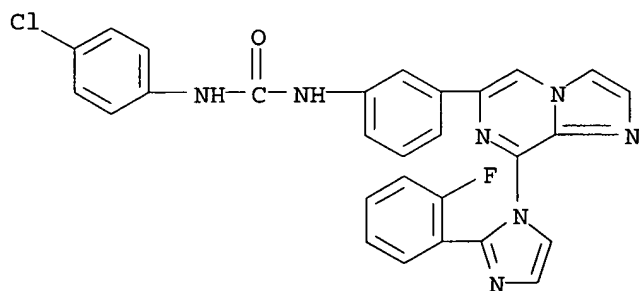
RN 746654-07-9 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[2-(2-methoxyphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



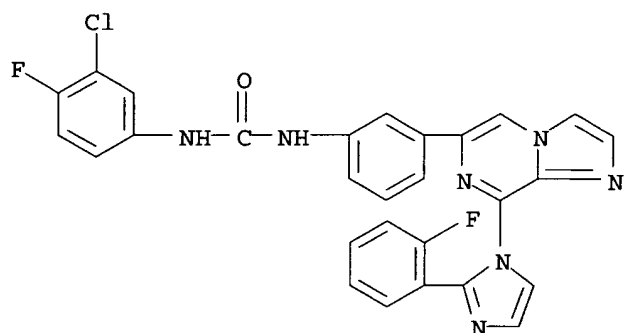
RN 746654-08-0 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[2-(2-fluorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



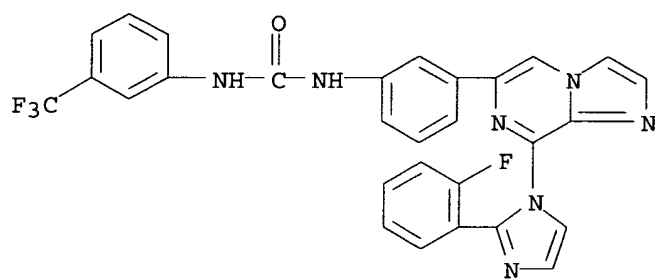
RN 746654-09-1 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[2-(2-fluorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



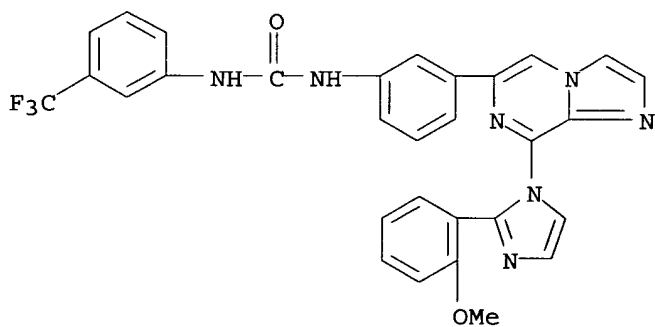
RN 746654-10-4 HCAPLUS

CN Urea, N-[3-[8-[2-(2-fluorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



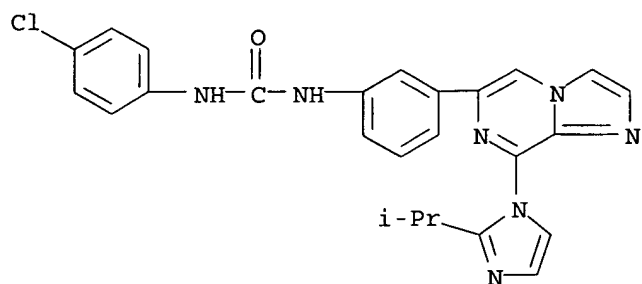
RN 746654-11-5 HCAPLUS

CN Urea, N-[3-[8-[2-(2-methoxyphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



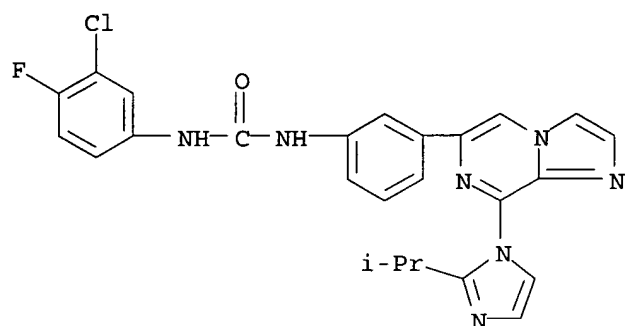
RN 746654-12-6 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[2-(1-methylethyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



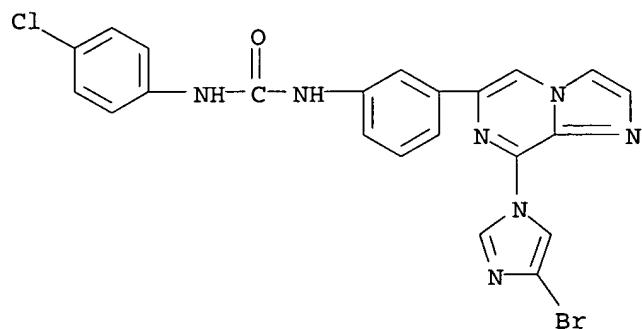
RN 746654-13-7 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[2-(1-methylethyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



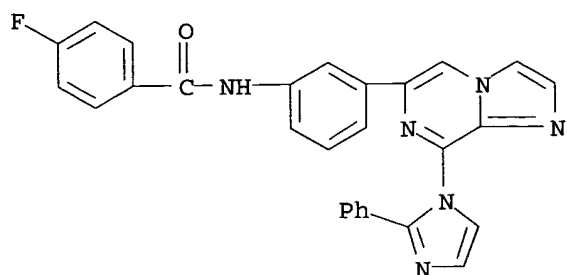
RN 746654-14-8 HCAPLUS

CN Urea, N-[3-[8-(4-bromo-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



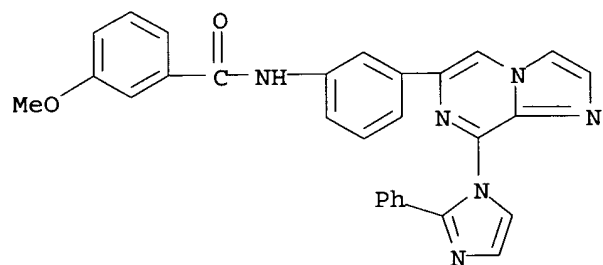
RN 746654-15-9 HCAPLUS

CN Benzamide, 4-fluoro-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



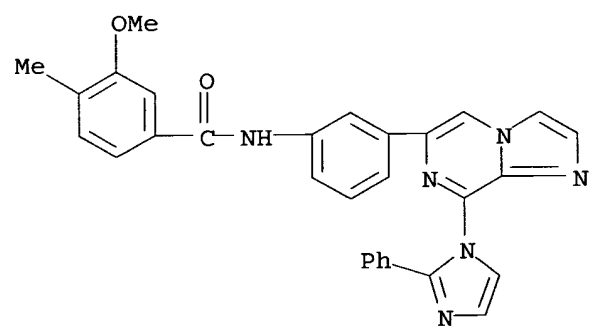
RN 746654-16-0 HCAPLUS

CN Benzamide, 3-methoxy-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



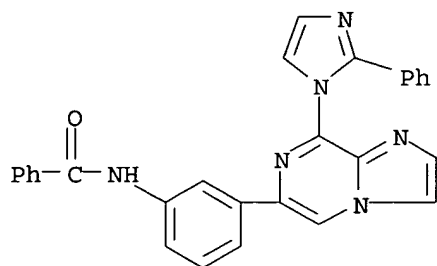
RN 746654-17-1 HCAPLUS

CN Benzamide, 3-methoxy-4-methyl-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



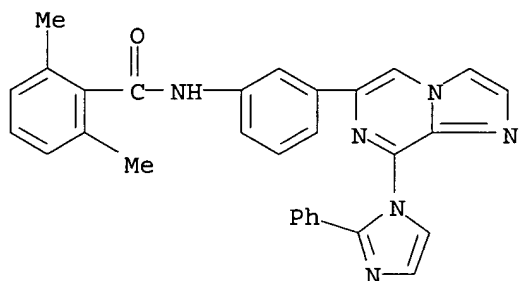
RN 746654-18-2 HCAPLUS

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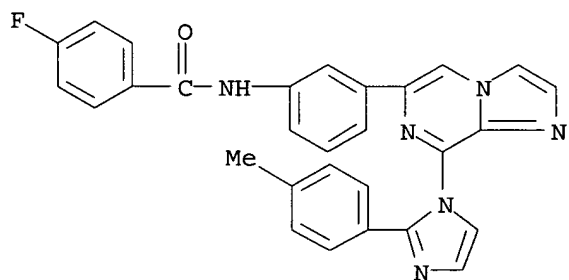
RN 746654-19-3 HCAPLUS

CN Benzamide, 2,6-dimethyl-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



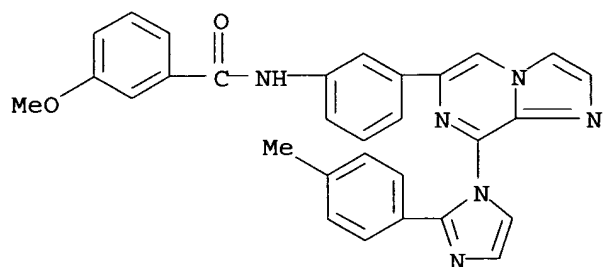
RN 746654-20-6 HCAPLUS

CN Benzamide, 4-fluoro-N-[3-[8-[2-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



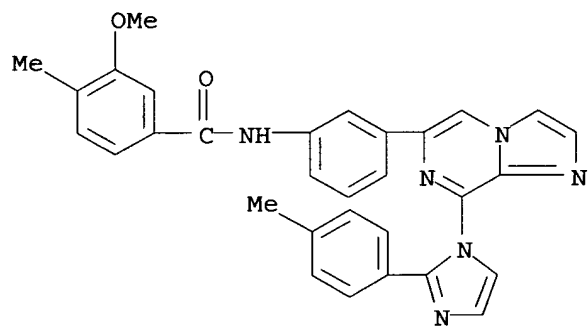
RN 746654-21-7 HCAPLUS

CN Benzamide, 3-methoxy-N-[3-[8-[2-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



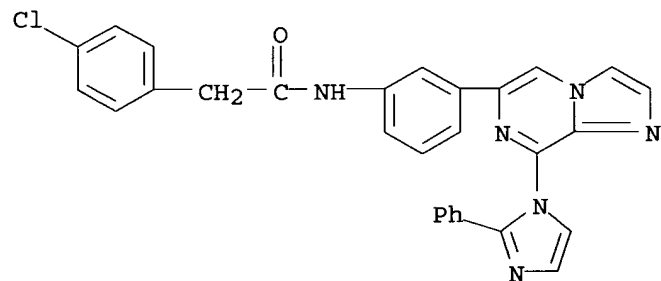
RN 746654-22-8 HCAPLUS

CN Benzamide, 3-methoxy-4-methyl-N-[3-[8-[2-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



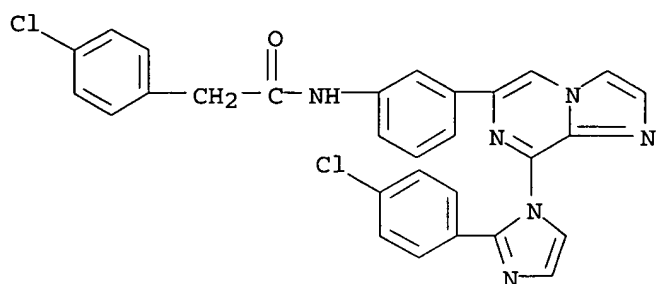
RN 746654-23-9 HCAPLUS

CN Benzeneacetamide, 4-chloro-N-[3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



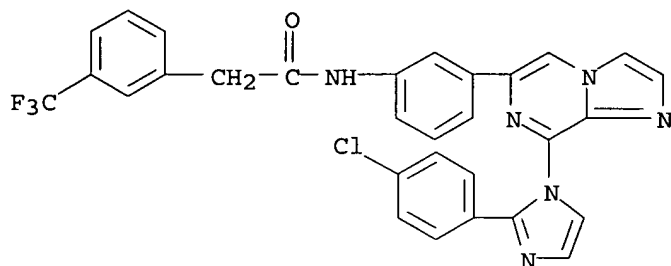
RN 746654-24-0 HCAPLUS

CN Benzeneacetamide, 4-chloro-N-[3-[8-[2-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



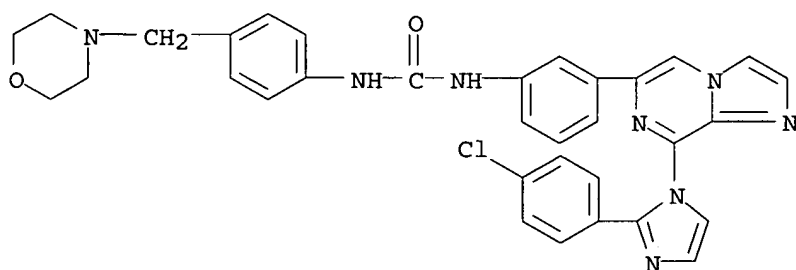
RN 746654-25-1 HCAPLUS

CN Benzeneacetamide, N-[3-[8-[2-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



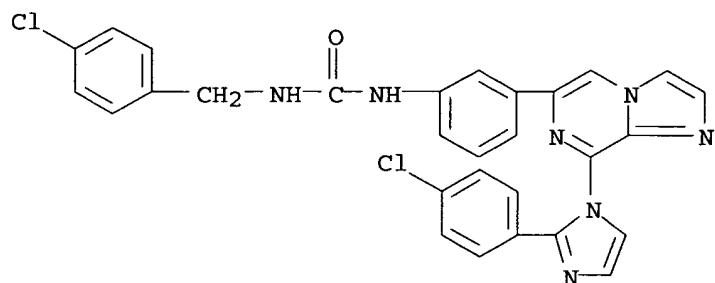
RN 746654-26-2 HCAPLUS

CN Urea, N-[3-[8-[2-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(4-morpholinylmethyl)phenyl]- (9CI) (CA INDEX NAME)



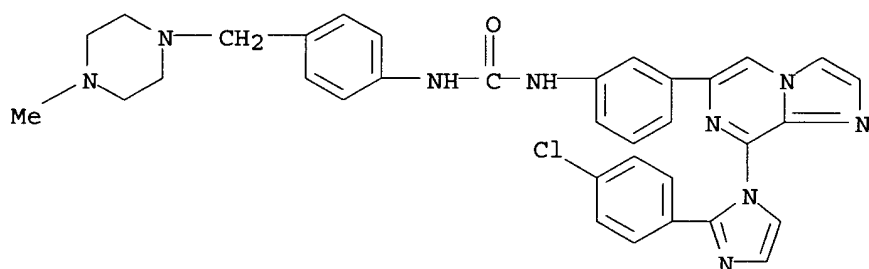
RN 746654-27-3 HCAPLUS

CN Urea, N-[3-[8-[2-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 746654-28-4 HCAPLUS

CN Urea, N-[3-[8-[2-(4-chlorophenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-[(4-methyl-1-piperazinyl)methyl]phenyl]- (9CI) (CA INDEX NAME)



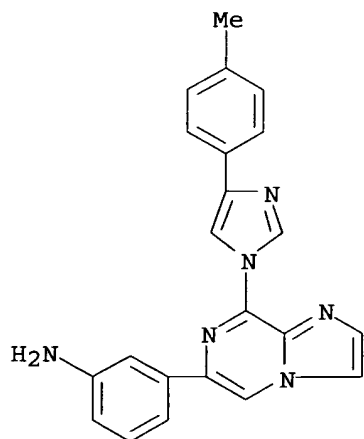
IT 746654-30-8P, 3-[8-(4-p-Tolylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenylamine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of heteroarylphenylimidazopyrazines as modulators of Hsp90 complex activity)

RN 746654-30-8 HCAPLUS

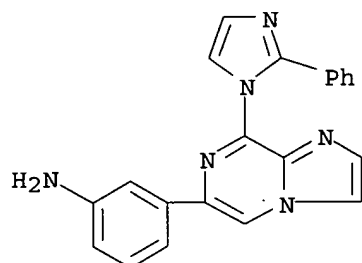
CN Benzenamine, 3-[8-[4-(4-methylphenyl)-1H-imidazol-1-yl]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



IT 746654-31-9, 3-[8-(2-Phenylimidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]phenylamine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (starting material; preparation of heteroarylphenylimidazopyrazines as modulators of Hsp90 complex activity)

RN 746654-31-9 HCAPLUS

CN Benzenamine, 3-[8-(2-phenyl-1H-imidazol-1-yl)imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:563869 HCAPLUS

DOCUMENT NUMBER: 141:260351

TITLE: Preparation of enantiopure biimidazoline ligands and their use in asymmetric catalysis

AUTHOR(S): Boland, Nicola A.; Casey, Mike; Hynes, Stephen J.; Matthews, Jonathan W.; Mueller-Bunz, Helge; Wilkes, Philippa

CORPORATE SOURCE: Chemistry Department, the Centre for Synthesis and Chemical Biology, the Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Ire.

SOURCE: Organic & Biomolecular Chemistry (2004), 2(14), 1995-2002

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:260351

AB A convenient new method for the preparation of 2,2'-biimidazolines is reported. Amino alcs. were reacted with di-Me oxalate, and the product hydroxy amides converted into chloro amides by reaction with thionyl chloride. Treatment with PCl5, followed by diamines (ethanediamine, propane-1,3-diamine, 2,2-dimethylpropane-1,3-diamine) furnished a series of enantiopure tricyclic biimidazolines. Complexes of two of the ligands with PdCl2 were prepared and their X-ray crystal structures were determined

The biimidazolines were tested as ligands for asym. Pd-catalyzed allylations. Moderate enantioselectivity ($\leq 80\%$ ee) was found for the reaction of di-Me malonate with diphenylallyl acetate, with the 5,7,5 fused tricyclic systems outperforming the 5,6,5 analogs. The corresponding reaction of pentenyl acetate gave lower enantioselectivity (44-57% ee), and proved very sensitive to the donor strength of the ligands, the stronger donors giving lower yields. The results provide a further demonstration of the value of the tunability of imidazoline ligands.

IT 754231-65-7P 754231-67-9P

RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation);

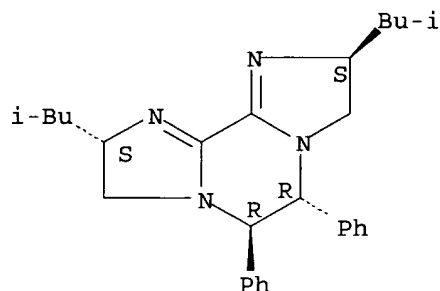
USES (Uses)

(preparation of enantiopure biimidazoline ligands as chiral ligands in asym. allylations)

RN 754231-65-7 HCAPLUS

CN Diimidazo[1,2-a:2',1'-c]pyrazine, 2,3,5,6,8,9-hexahydro-2,9-bis(2-methylpropyl)-5,6-diphenyl-, (2S,5R,6R,9S)- (9CI) (CA INDEX NAME)

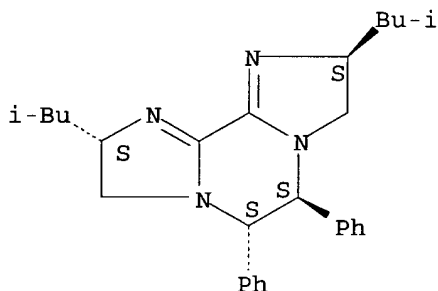
Absolute stereochemistry.



RN 754231-67-9 HCAPLUS

CN Diimidazo[1,2-a:2',1'-c]pyrazine, 2,3,5,6,8,9-hexahydro-2,9-bis(2-methylpropyl)-5,6-diphenyl-, (2S,5S,6S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267339 HCAPLUS

DOCUMENT NUMBER: 140:303700

TITLE: Preparation and pharmaceutical compositions of novel imidazopyrazines as cyclin dependent kinase inhibitors
 INVENTOR(S): Paruch, Kamil; Guzi, Timothy J.; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Mallams, Alan K.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

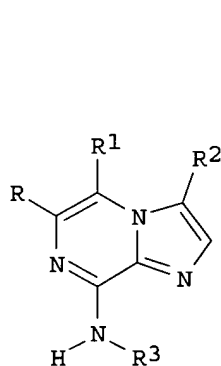
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FAMILY ACC. NUM. COUNT: 1

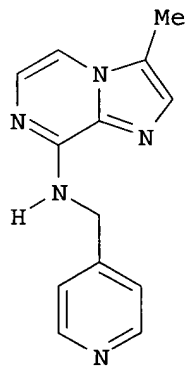
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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WO 2004026877 A1 20040401 WO 2003-US29209 20030919
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HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA,
MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC,
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PRIORITY APPLN. INFO.: US 2002-412997P P 20020923
US 2003-665005 A3 20030919
WO 2003-US29209 W 20030919
OTHER SOURCE(S): MARPAT 140:303700
GI



I



II

AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R1 = H, halo or alkyl; R2 = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R3 = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-a]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC50 value of 22.5 μ M.

IT 676359-71-0P 676359-73-2P 676359-74-3P
676359-76-5P 676359-78-7P 676359-80-1P

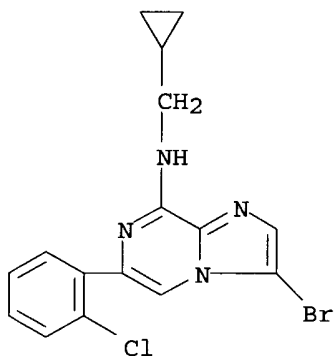
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 676360-57-9P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(drug candidate; combinatorial preparation of a library of imidazopyrazines as cyclin dependent kinase inhibitors)

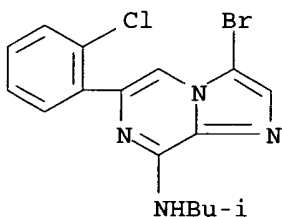
RN 676359-71-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(cyclopropylmethyl)- (9CI) (CA INDEX NAME)



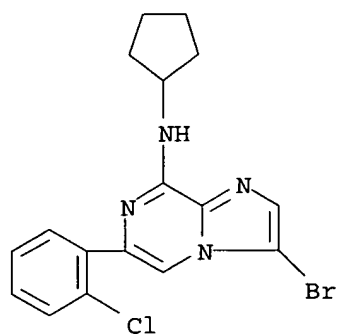
RN 676359-73-2 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(2-methylpropyl)- (9CI) (CA INDEX NAME)



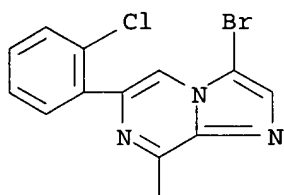
RN 676359-74-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-cyclopentyl- (9CI) (CA INDEX NAME)



RN 676359-76-5 HCAPLUS

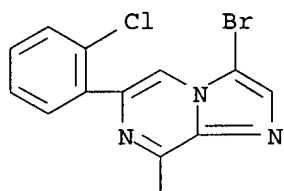
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)



Me₂CH-CH₂-CH₂-NH

RN 676359-78-7 HCAPLUS

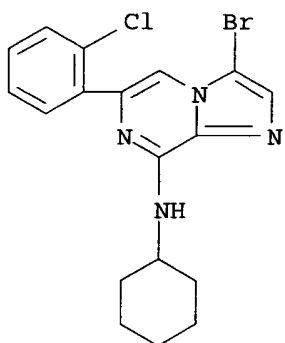
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-methoxypropyl)- (9CI) (CA INDEX NAME)



MeO-(CH₂)₃-NH

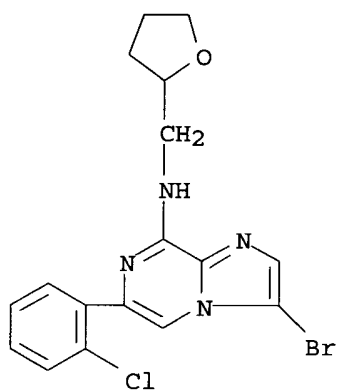
RN 676359-80-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-cyclohexyl- (9CI) (CA INDEX NAME)



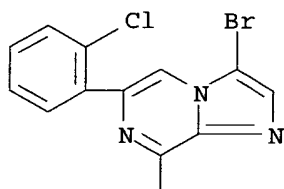
RN 676359-82-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



RN 676359-84-5 HCAPLUS

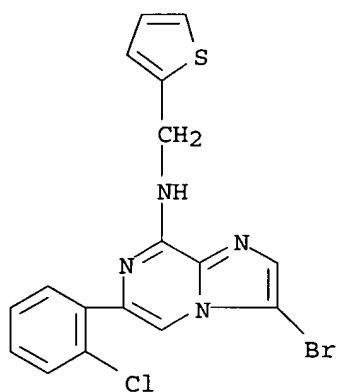
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-ethoxypropyl)- (9CI) (CA INDEX NAME)



EtO—(CH₂)₃—NH

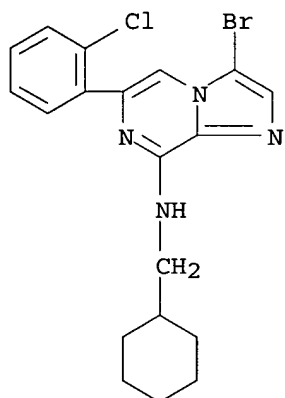
RN 676359-86-7 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



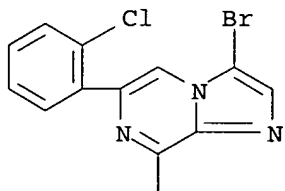
RN 676359-88-9 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(cyclohexylmethyl)- (9CI) (CA INDEX NAME)



RN 676359-90-3 HCAPLUS

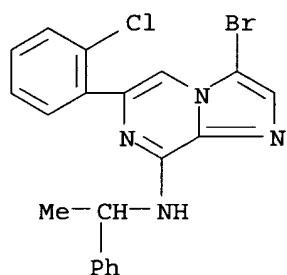
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1-methylethoxy)propyl]- (9CI) (CA INDEX NAME)



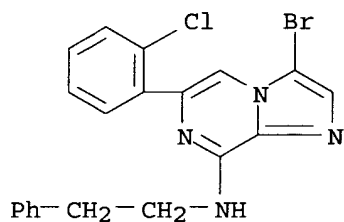
i-PrO-(CH₂)₃-NH

RN 676359-92-5 HCAPLUS

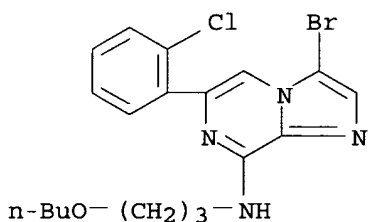
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(1-phenylethyl)- (9CI) (CA INDEX NAME)



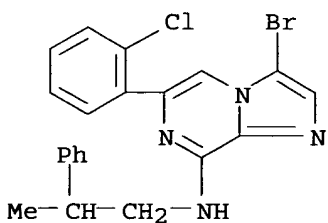
RN 676359-94-7 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 676359-96-9 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-(3-butoxypropyl)-6-(2-chlorophenyl)- (9CI) (CA INDEX NAME)

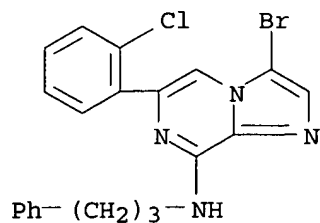


RN 676359-98-1 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(2-phenylpropyl)- (9CI) (CA INDEX NAME)



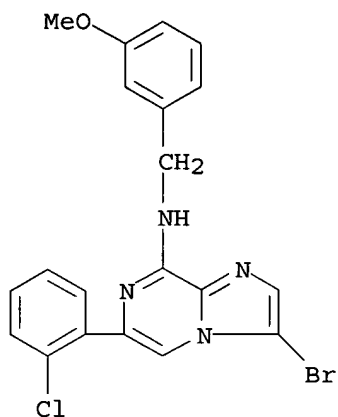
RN 676359-99-2 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-

phenylpropyl)- (9CI) (CA INDEX NAME)



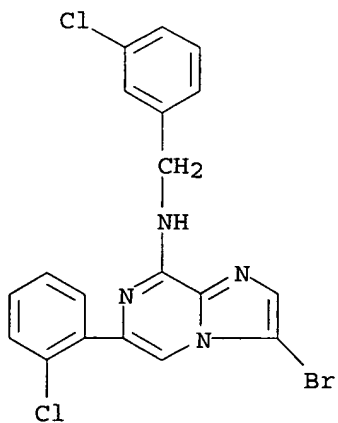
RN 676360-00-2 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



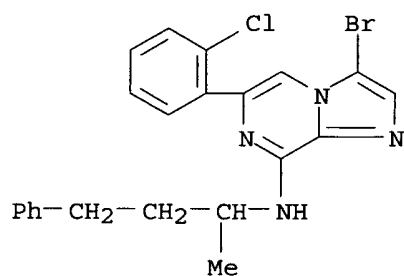
RN 676360-02-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(3-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)



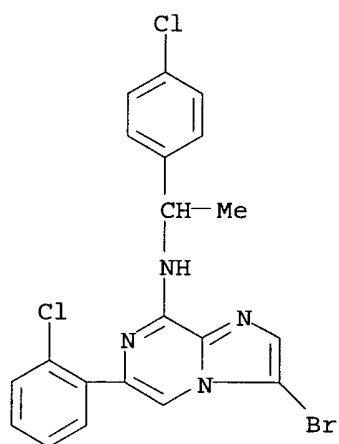
RN 676360-03-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(1-methyl-3-phenylpropyl)- (9CI) (CA INDEX NAME)



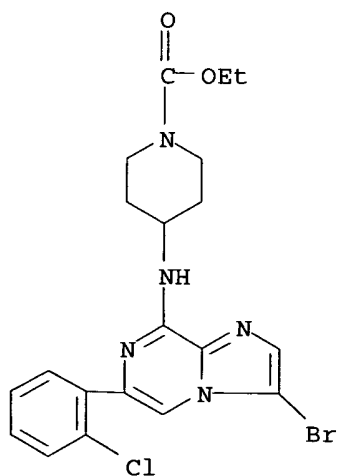
RN 676360-05-7 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[1-(4-chlorophenyl)ethyl]- (9CI) (CA INDEX NAME)



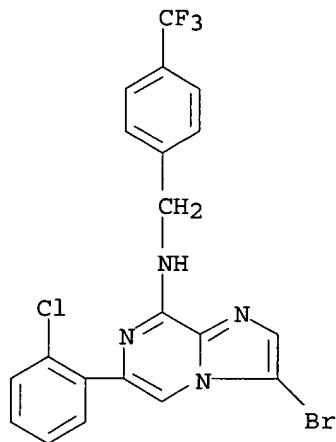
RN 676360-07-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



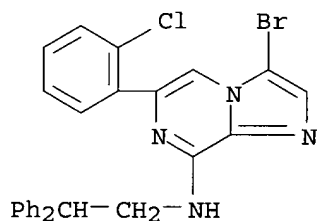
RN 676360-09-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



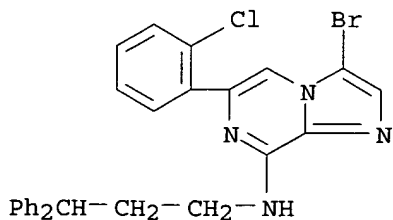
RN 676360-11-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(2,2-diphenylethyl)- (9CI) (CA INDEX NAME)



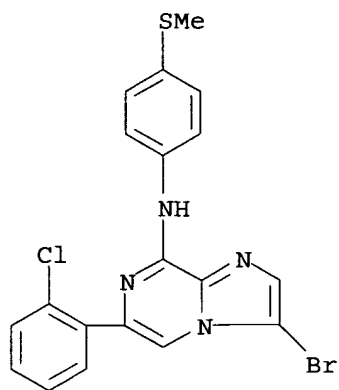
RN 676360-13-7 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3,3-diphenylpropyl)- (9CI) (CA INDEX NAME)



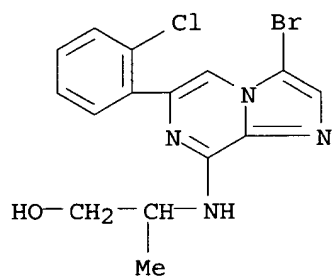
RN 676360-15-9 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[4-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



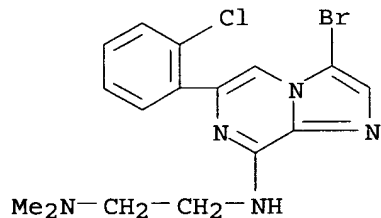
RN 676360-17-1 HCAPLUS

CN 1-Propanol, 2-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



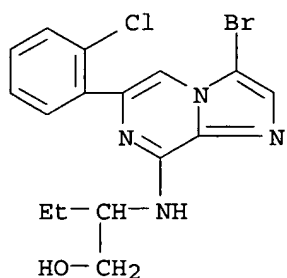
RN 676360-19-3 HCAPLUS

CN 1,2-Ethanediamine, N'-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N,N-dimethyl-(9CI) (CA INDEX NAME)



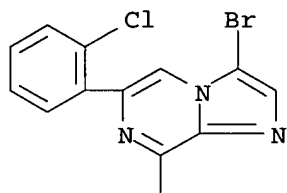
RN 676360-21-7 HCAPLUS

CN 1-Butanol, 2-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



RN 676360-23-9 HCAPLUS

CN 1,3-Propanediamine, N'-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

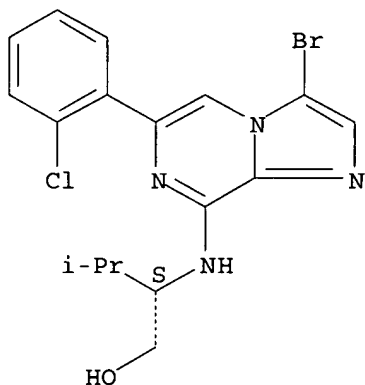


Me₂N- (CH₂)₃-NH

RN 676360-25-1 HCAPLUS

CN 1-Butanol, 2-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3-methyl-, (2S)- (9CI) (CA INDEX NAME)

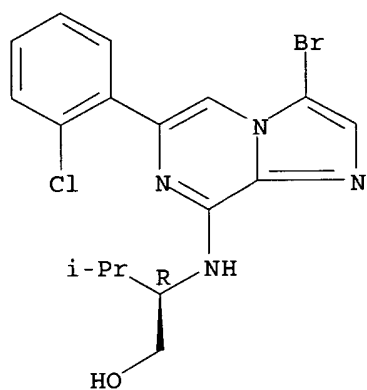
Absolute stereochemistry.



RN 676360-27-3 HCAPLUS

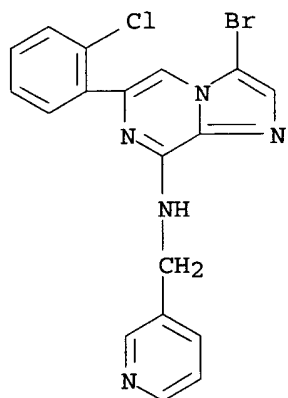
CN 1-Butanol, 2-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



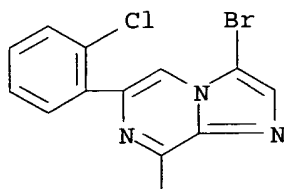
RN 676360-29-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 676360-31-9 HCAPLUS

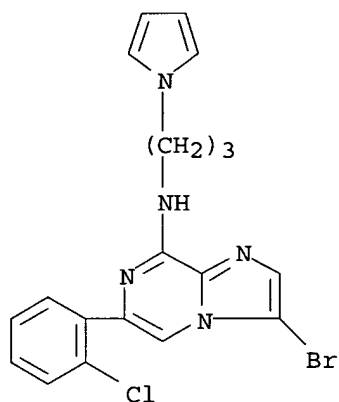
CN 1,2-Ethanediamine, N'-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N,N-diethyl- (9CI) (CA INDEX NAME)



Et₂N-CH₂-CH₂-NH

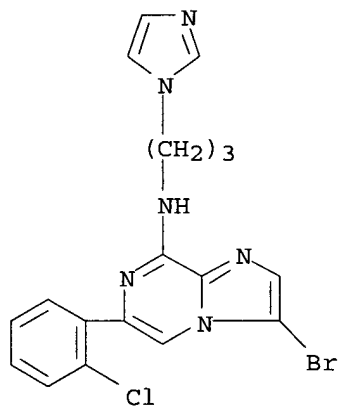
RN 676360-33-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1H-pyrrol-1-yl)propyl]- (9CI) (CA INDEX NAME)



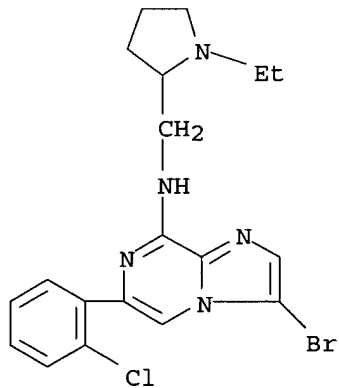
RN 676360-35-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



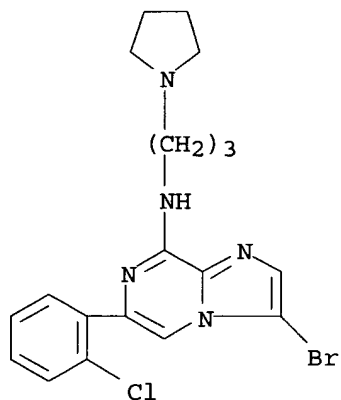
RN 676360-37-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



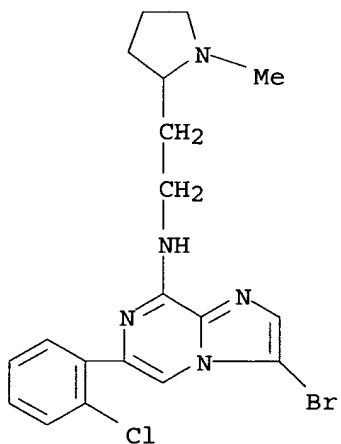
RN 676360-39-7 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)



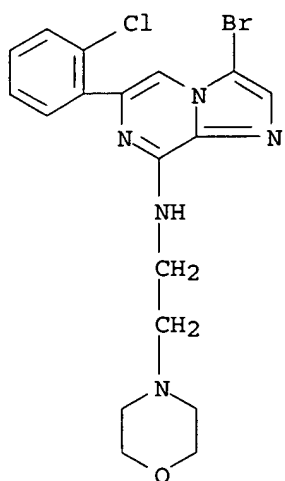
RN 676360-41-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(1-methyl-2-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



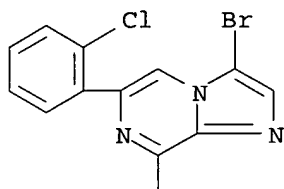
RN 676360-43-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 676360-45-5 HCAPLUS

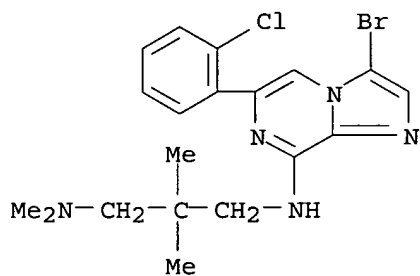
CN 1,3-Propanediamine, N'-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N,N-diethyl- (9CI) (CA INDEX NAME)



Et₂N-(CH₂)₃-NH

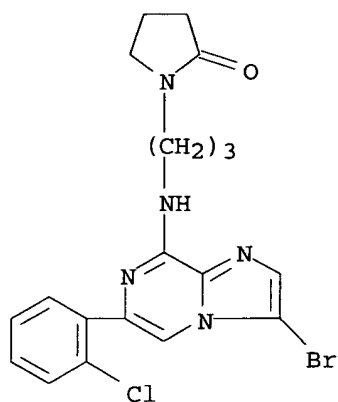
RN 676360-47-7 HCAPLUS

CN 1,3-Propanediamine, N'-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-N,N,2,2-tetramethyl- (9CI) (CA INDEX NAME)



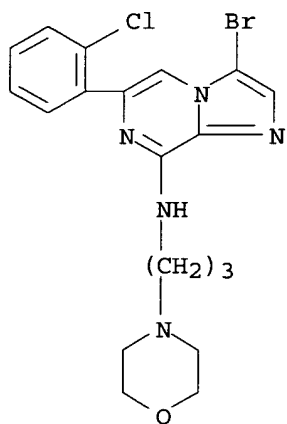
RN 676360-49-9 HCAPLUS

CN 2-Pyrrolidinone, 1-[3-[[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]propyl]- (9CI) (CA INDEX NAME)



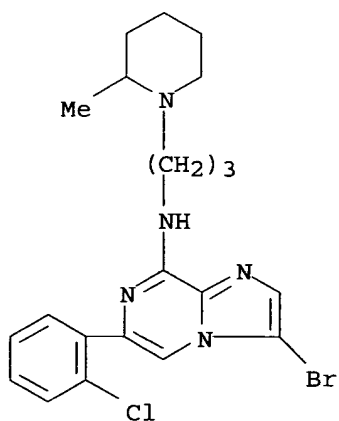
RN 676360-51-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

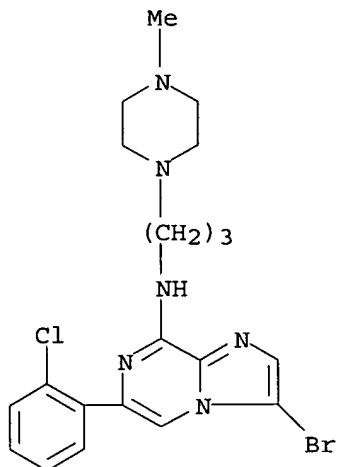


RN 676360-53-5 HCAPLUS

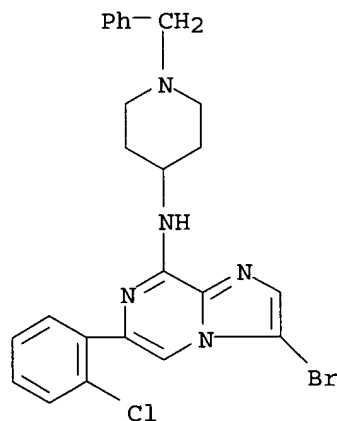
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(2-methyl-1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



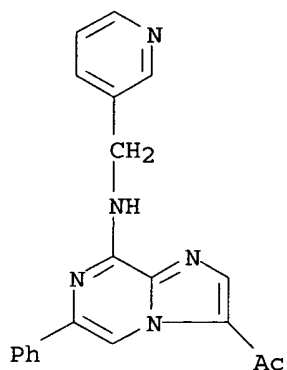
RN 676360-55-7 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



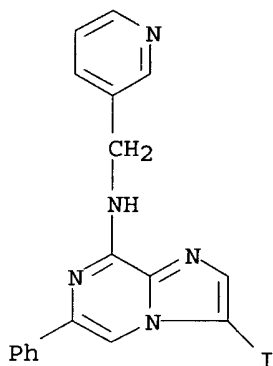
RN 676360-57-9 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-[1-(phenylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



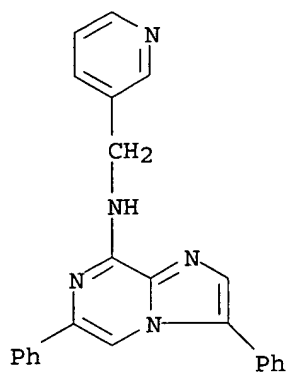
IT **676359-53-8P 676360-96-6P**
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (drug candidate; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)
 RN 676359-53-8 HCAPLUS
 CN Ethanone, 1-[6-phenyl-8-[(3-pyridinylmethyl) amino]imidazo[1,2-a]pyrazin-3-yl]- (9CI) (CA INDEX NAME)



RN 676360-96-6 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(3-pyridinylmethyl)-
 (9CI) (CA INDEX NAME)

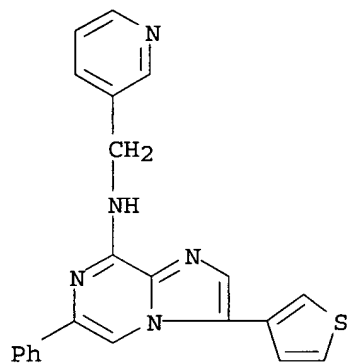


IT 676359-47-0P 676359-49-2P 676359-51-6P
 676359-55-0P 676359-70-9P 676360-67-1P
 676360-69-3P 676360-71-7P 676360-73-9P
 676360-76-2P 676360-78-4P 676360-80-8P
 676360-82-0P 676360-84-2P 676360-86-4P
 676360-89-7P 676360-91-1P 676360-93-3P
 676360-94-4P 676360-98-8P 676361-00-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (drug candidate; preparation of imidazopyrazines as cyclin dependent kinase
 inhibitors)
 RN 676359-47-0 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3,6-diphenyl-N-(3-pyridinylmethyl)- (9CI)
 (CA INDEX NAME)



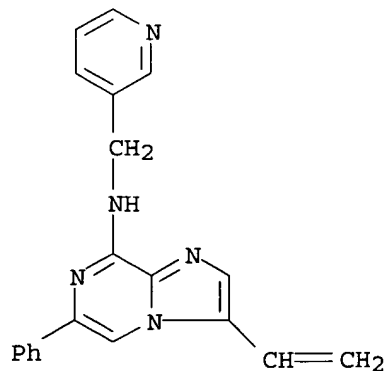
RN 676359-49-2 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl-N-(3-pyridinylmethyl)-3-(3-thienyl)- (9CI) (CA INDEX NAME)



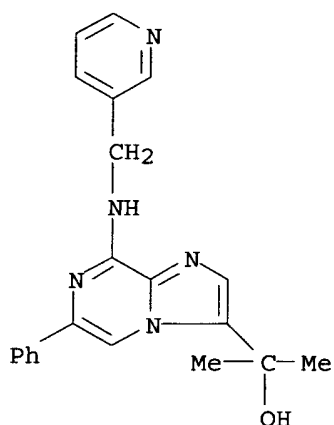
RN 676359-51-6 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-ethenyl-6-phenyl-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



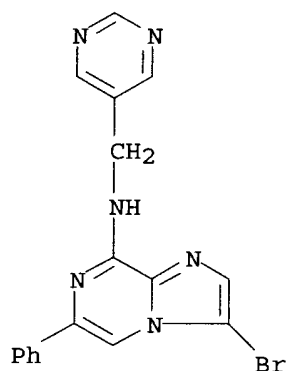
RN 676359-55-0 HCAPLUS

CN Imidazo[1,2-a]pyrazine-3-methanol, α,α -dimethyl-6-phenyl-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



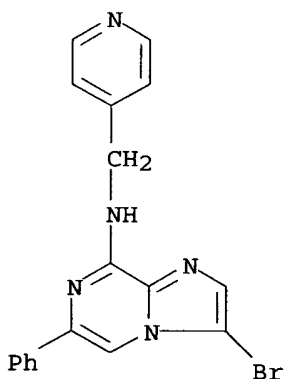
RN 676359-70-9 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(5-pyrimidinylmethyl)-
(9CI) (CA INDEX NAME)



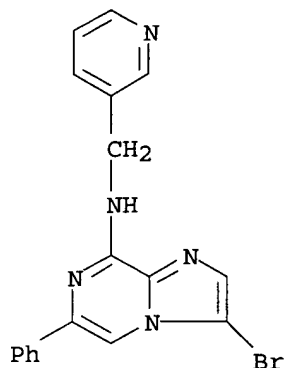
RN 676360-67-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(4-pyridinylmethyl)-
(9CI) (CA INDEX NAME)

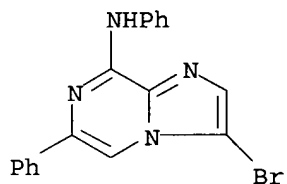


RN 676360-69-3 HCAPLUS

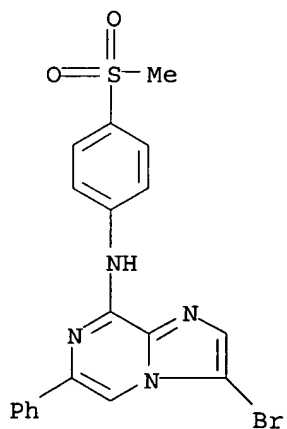
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-(3-pyridinylmethyl)-
(9CI) (CA INDEX NAME)



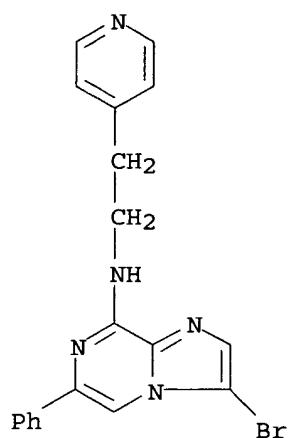
RN 676360-71-7 HCAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N,6-diphenyl- (9CI) (CA INDEX NAME)



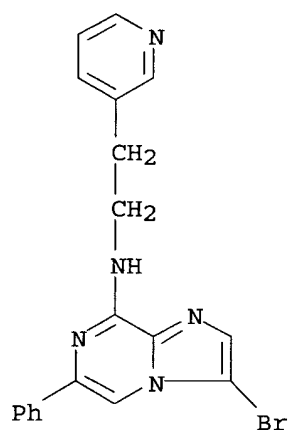
RN 676360-73-9 HCAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-[4-(methylsulfonyl)phenyl]-6-phenyl- (9CI) (CA INDEX NAME)



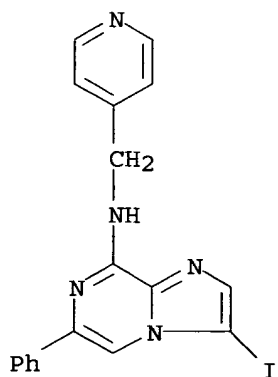
RN 676360-76-2 HCAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(4-pyridinyl)ethyl]-
(9CI) (CA INDEX NAME)



RN 676360-78-4 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[2-(3-pyridinyl)ethyl]-
 (9CI) (CA INDEX NAME)

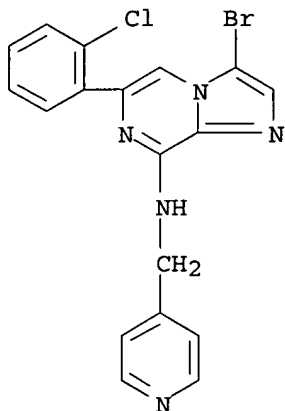


RN 676360-80-8 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 3-iodo-6-phenyl-N-(4-pyridinylmethyl)-
 (9CI) (CA INDEX NAME)



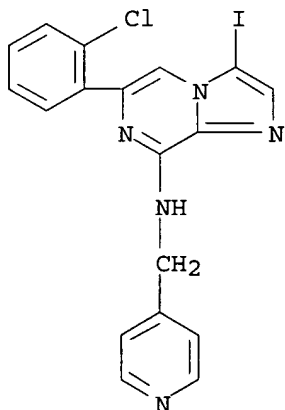
RN 676360-82-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-(2-chlorophenyl)-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



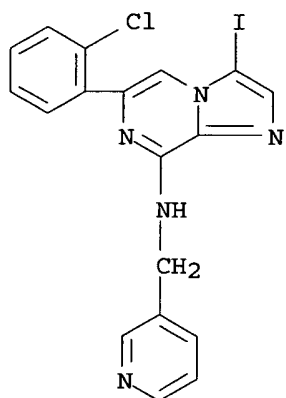
RN 676360-84-2 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



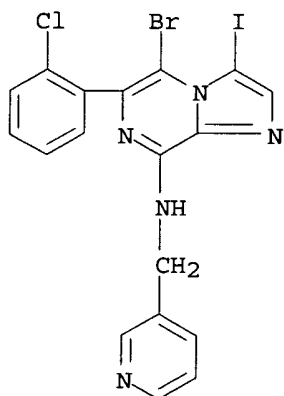
RN 676360-86-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



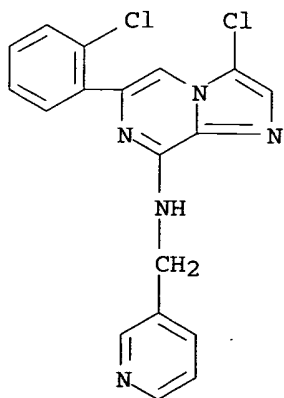
RN 676360-89-7 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 5-bromo-6-(2-chlorophenyl)-3-iodo-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



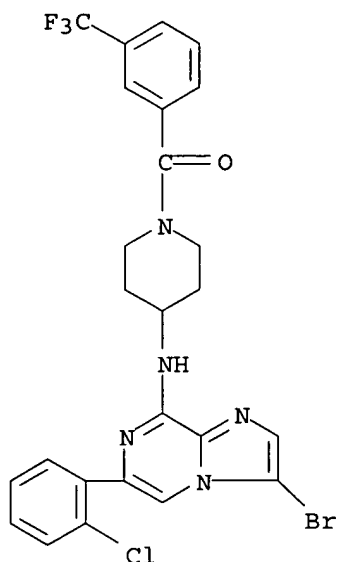
RN 676360-91-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-chloro-6-(2-chlorophenyl)-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



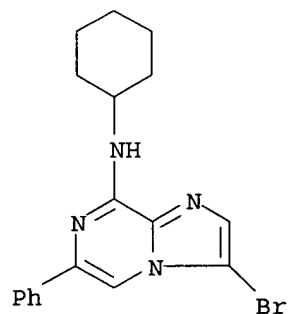
RN 676360-93-3 HCAPLUS

CN 4-Piperidinamine, N-[3-bromo-6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]-
1-[3-(trifluoromethyl)benzoyl]- (9CI) (CA INDEX NAME)



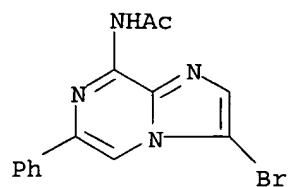
RN 676360-94-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-N-cyclohexyl-6-phenyl- (9CI) (CA INDEX NAME)



RN 676360-98-8 HCAPLUS

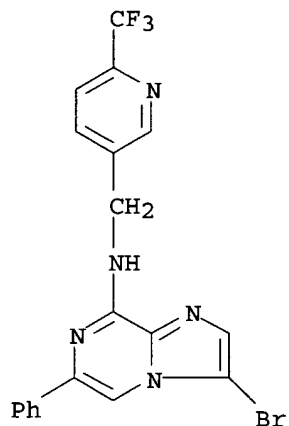
CN Acetamide, N-(3-bromo-6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



RN 676361-00-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl-N-[[6-(trifluoromethyl)-3-

pyridinyl)methyl]- (9CI) (CA INDEX NAME)



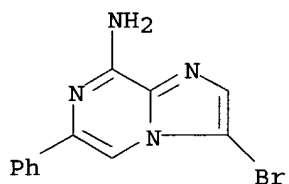
IT 676361-13-0P 676361-14-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)

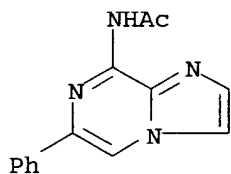
RN 676361-13-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 3-bromo-6-phenyl- (9CI) (CA INDEX NAME)



RN 676361-14-1 HCAPLUS

CN Acetamide, N-(6-phenylimidazo[1,2-a]pyrazin-8-yl)- (9CI) (CA INDEX NAME)



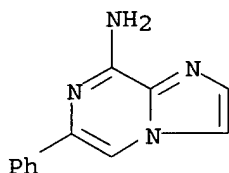
IT 673857-28-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of imidazopyrazines as cyclin dependent kinase inhibitors)

RN 673857-28-8 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:220337 HCAPLUS

DOCUMENT NUMBER: 140:270878

TITLE: Kinase-modulating 6-aryl-imidazo[1,2-a]pyrazin-8-ylamines, method of their preparation, and method of their use, e.g., against cancer cells

INVENTOR(S): Desimone, Robert W.; Pippin, Douglas A.; Darrow, James W.; Mitchell, Scott A.; Currie, Kevin S.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2004022562 | A1 | 20040318 | WO 2003-US28329 | 20030909 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2003270489 | A1 | 20040329 | AU 2003-270489 | 20030909 |
| US 2004067951 | A1 | 20040408 | US 2003-658121 | 20030909 |
| PRIORITY APPLN. INFO.: | | | US 2002-409161P | P 20020909 |
| | | | WO 2003-US28329 | W 20030909 |

OTHER SOURCE(S): MARPAT 140:270878

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, cycloalkylmethyl, (hetero)(cyclo)alkyl, sulfonamide, alkoxy, alkoxyalkoxy, alkoxyalkyl, (di)(alkyl)amino(alkyl), (un)substituted Ph or heteroaryl; R2 = (hetero)(cyclo)alkyl, cycloalkylmethyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, (di)(alkyl)amino(alkyl), (un)substituted Ph, heteroaryl, phenoxyphenyl, phenyl- or heteroarylpiperazine; R3 = H, CO2H or esters, (hetero)(cyclo)alkyl, (un)substituted Ph, heteroaryl, phenoxyphenyl,

phenyl- or heteroaryl piperazine; R4 = H, (hetero)(cyclo)alkyl, alkoxyalkyl, (un)substituted Ph, heteroaryl, phenoxyphenyl, phenyl- or heteroaryl piperazine; X = N or CH; Z1 = bond, CO, (un)substituted CH2, CH2CH2, CONH; Z2 = bond, CO, (un)substituted CH2NHCONH, NHCONHCH2, CH2, CH2CH2, CONH, NHCO, NHCONH, SO2NH, NHSO2; some substituents may be linked; with provisos] and their pharmaceutically acceptable salts, hydrates, solvates, crystal forms, diastereomers, prodrugs, or mixts., are disclosed. Compds. I are of particular utility in the treatment of kinase-implicated disorders. A list of 91 invention compds. is given in examples, and the compds. are individually claimed. A general preparatory method starting from 3,5-dibromo-2-aminopyrazine is given; the steps include (among others) cyclocondensation with α -bromo aldehydes, monoaminolysis of the resultant 6,8-dibromoimidazopyrazines, Pd-catalyzed arylation of the obtained 8-amino-6-bromoimidazopyrazines, and reaction of 6-(aminophenyl)imidazolpyrazines with Ph isocyanate derivs. to form ureas. An exemplary invention compound is II. In tests against human cancer cell lines, including one over-expressing transfected human myrAKT-1 kinase gene (AKT-1 kinase), exemplified compds. I had IC50 values ≤ 25 μ M.

IT **618454-80-1P**, 1-(4-Chlorophenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea **618454-86-7P**, 1-(4-Chlorophenyl)-3-[3-[8-(4-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **618454-91-4P**, 1-(4-Chlorophenyl)-3-[3-[8-(3-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **618455-30-4P**, 4-[6-[3-[3-(4-Chlorophenyl)ureido]phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester **618455-54-2P**, 1-[4-[8-(2-Methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-phenylurea **618455-60-0P**, (2-Methoxybenzyl)[6-[3-(4-methoxybenzylamino)phenyl]imidazo[1,2-a]pyrazin-8-yl]amine **618455-66-6P**, 1-(2-Chlorophenyl)-3-[4-[8-(2-methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **618455-69-9P**, 1-[4-[8-(2-Methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxyphenyl)urea **618455-71-3P**, 1-[4-[8-(2-Methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-methoxyphenyl)urea **618455-73-5P**, 4-[6-[4-(Piperidine-1-carbonyl)phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester **618455-75-7P**, 4-[6-[3-[3-(2-Methylsulfonylphenyl)ureido]phenyl]imidazo[1,2-a]pyrazin-8-ylamino]benzoic acid ethyl ester **618455-77-9P**, [4-[8-(4-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]piperidin-1-ylmethanone **618455-84-8P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea **618455-86-0P**, 1-[3-(8-Phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]-3-(3-trifluoromethylphenyl)urea **618455-88-2P**, 1-(2-Chloro-5-trifluoromethylphenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl)phenyl]urea **618455-91-7P**, 1-[3-[8-(4-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **618455-94-0P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(3-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **618455-97-3P**, 1-[3-[8-(3-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **618455-99-5P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(2-chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673856-56-9P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-chlorophenyl)urea **673856-57-0P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-chlorophenyl)urea **673856-58-1P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxyphenyl)urea **673856-59-2P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-

chlorophenyl)urea **673856-60-5P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-61-6P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-trifluoromethylphenyl)urea **673856-62-7P**, 1-[4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-trifluoromethoxyphenyl)urea **673856-63-8P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methylsulfanylphenyl)urea **673856-64-9P**, 1-[3-[8-[Methyl(4-methylbenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methylsulfanylphenyl)urea **673856-65-0P**, 1-(4-Chlorophenyl)-3-[3-[8-[methyl(4-methylbenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673856-66-1P**, 1-[3-[8-[Methyl(4-methylbenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-67-2P**, 1-(4-Chlorophenyl)-3-[3-[8-(3,4-dihydro-1H-isoquinolin-2-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673856-68-3P**, 1-[3-[8-(3,4-Dihydro-1H-isoquinolin-2-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methylsulfanylphenyl)urea **673856-69-4P**, 1-[3-[8-(3,4-Dihydro-1H-isoquinolin-2-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-70-7P**, 1-[3-[8-(3,4-Dihydro-1H-isoquinolin-2-yl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxyphenyl)urea **673856-71-8P**, 8-[(4-Chlorobenzyl)methylamino]-6-[3-[3-(2-trifluoromethylphenyl)ureido]phenyl]imidazo[1,2-a]pyrazine-3-carboxylic acid ethyl ester **673856-72-9P**, 8-[(4-Chlorobenzyl)methylamino]-6-[3-(3-o-tolylureido)phenyl]imidazo[1,2-a]pyrazine-3-carboxylic acid ethyl ester **673856-73-0P**, 8-[(4-Chlorobenzyl)methylamino]-6-[3-[3-(4-chlorophenyl)ureido]phenyl]imidazo[1,2-a]pyrazine-3-carboxylic acid ethyl ester **673856-74-1P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[methyl(4-methylbenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673856-75-2P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-chloro-4-fluorophenyl)urea **673856-76-3P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]benzyl]-3-(4-chlorophenyl)urea **673856-77-4P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]benzyl]-3-(3-chloro-4-fluorophenyl)urea **673856-78-5P**, 1-[3-[8-[(4-Chlorobenzyl)ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-79-6P**, 1-[3-[8-[(4-Chlorobenzyl)ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-80-9P**, 1-[3-[8-[(4-Chlorobenzyl)ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-chloro-4-fluorophenyl)urea **673856-81-0P**, 1-[3-[8-[(4-Chlorobenzyl)propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-82-1P**, 1-[3-[8-[(4-Chlorobenzyl)propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-chloro-4-fluorophenyl)urea **673856-83-2P**, 1-[3-[8-[Butyl(4-chlorobenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-84-3P**, 1-[3-[8-[(4-Chlorobenzyl)propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-85-4P**, 1-[3-[8-[(4-Chlorobenzyl)propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673856-86-5P**, 1-[3-[8-[Butyl(4-chlorobenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-87-6P**, 1-[3-[8-[Butyl(4-chlorobenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673856-88-7P**, 1-[3-[8-[Butyl(4-chlorobenzyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-chloro-4-fluorophenyl)urea **673856-89-8P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673856-90-1P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-o-tolylurea **673856-91-2P**, 1-[3-[8-(Benzylmethylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-92-3P**,

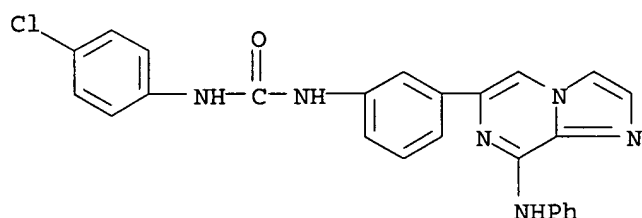
1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-trifluoromethoxyphenyl)urea **673856-93-4P**,
 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(5-fluoro-2-trifluoromethylphenyl)urea **673856-94-5P**,
 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3,5-dichlorophenyl)urea **673856-95-6P**, 1-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3,4-dichlorophenyl)urea **673856-96-7P**, 1-[3-[8-[(2-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673856-97-8P**, 1-[3-[8-[Methyl(pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673856-98-9P**, 1-(4-Chlorobenzyl)-3-[3-[8-[(4-chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673856-99-0P**, 1-[3-[8-[(4-Chlorobenzyl)(2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chlorophenyl)urea **673857-00-6P**, 1-[3-[8-[(4-Chlorobenzyl)(2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673857-01-7P**, 1-[3-[8-[(4-Chlorobenzyl)(2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-chloro-3-fluorophenyl)urea **673857-02-8P**, 1-[3-[8-[(4-Chlorobenzyl)(2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-[4-(4-methylpiperazin-1-ylmethyl)phenyl]urea **673857-03-9P**,
 N-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzenesulfonamide **673857-04-0P**, N-[3-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **673857-05-1P**, 4-Chloro-N-[3-[8-[(4-chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **673857-06-2P**,
 2-Chloro-N-[3-[8-[(4-chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **673857-07-3P**, [4-[8-[(3-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]piperidin-1-ylmethanone **673857-08-4P**, [4-[8-[(4-Chlorobenzyl)methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]piperidin-1-ylmethanone **673857-09-5P**, 3-Methoxy-N-[3-[8-(2-methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **673857-10-8P**, 2-Methoxy-N-[3-[8-(2-methoxybenzylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]benzamide **673857-11-9P**,
 1-[3-(8-Phenylaminoimidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(4-trifluoromethylphenyl)urea **673857-12-0P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-13-1P**, 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-3-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-14-2P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-3-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-15-3P**,
 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-16-4P**, 1-[3-[8-[(Pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673857-17-5P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-[(pyridin-4-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-18-6P**, 1-[3-[8-(Pyridin-4-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673857-19-7P** **673857-20-0P**, 1-(4-Chlorophenyl)-3-[3-[8-[(pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-21-1P**, 1-[3-[8-[(Pyridin-2-ylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673857-22-2P**, 1-(2-Methoxy-6-methylphenyl)-3-[3-[8-(pyridin-4-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-23-3P**,
 1-(2-Methoxy-5-methylphenyl)-3-[3-(8-phenylaminoimidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-24-4P**, 1-[3-[8-(3-Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxy-5-methylphenyl)urea **673857-25-5P**, 1-[3-[8-(2-

Chlorophenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(2-methoxy-5-methylphenyl)urea **673857-26-6P**, 1-[3-[8-(Pyridin-3-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-3-(3-trifluoromethylphenyl)urea **673857-27-7P**, 1-(3-Chloro-4-fluorophenyl)-3-[3-[8-(pyridin-3-ylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]urea **673857-29-9DP**, 1-[4-(8-Aminoimidazo[1,2-a]pyrazin-6-yl)phenyl]-3-phenylurea, derivs.
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of arylimidazopyrazinylamines as kinase modulators)

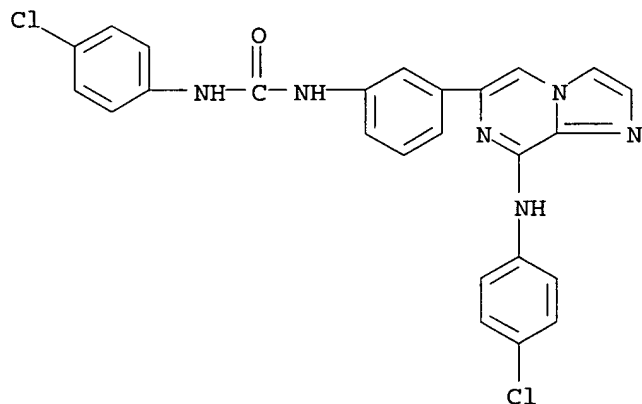
RN 618454-80-1 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



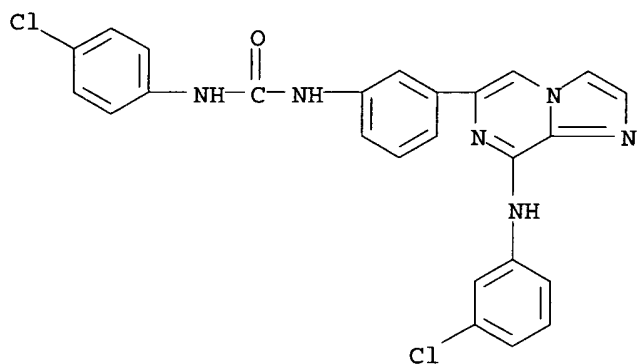
RN 618454-86-7 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



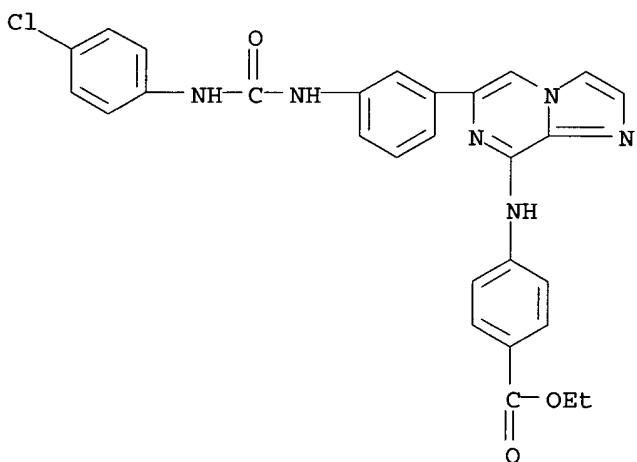
RN 618454-91-4 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



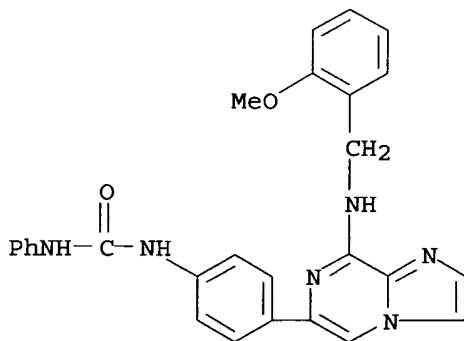
RN 618455-30-4 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 618455-54-2 HCAPLUS

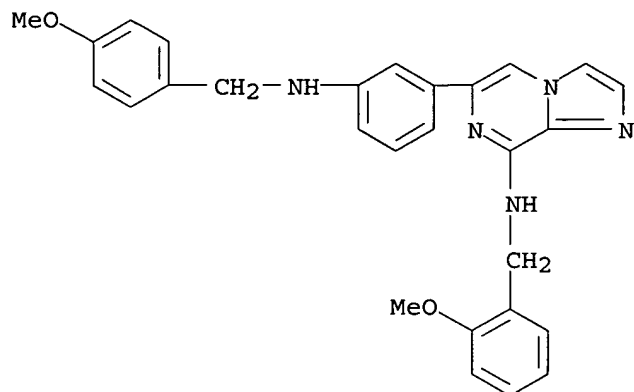
CN Urea, N-[4-[8-[[[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-phenyl]- (9CI) (CA INDEX NAME)



RN 618455-60-0 HCAPLUS

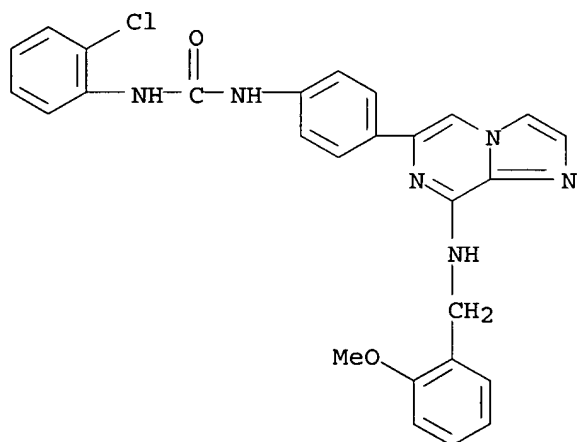
CN Imidazo[1,2-a]pyrazin-8-amine, N-[(2-methoxyphenyl)methyl]-6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]-

methoxyphenyl)methyl] amino]phenyl] - (9CI) (CA INDEX NAME)



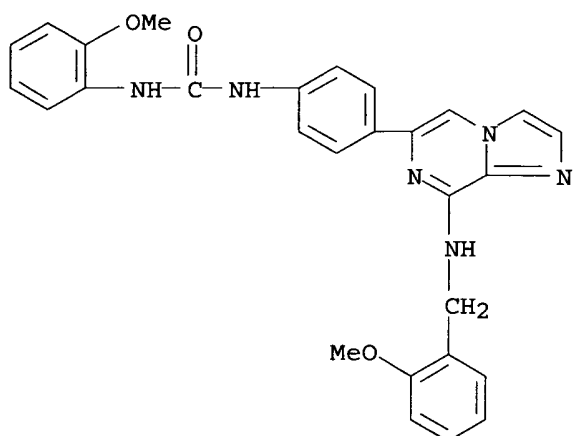
RN 618455-66-6 HCAPLUS

CN Urea, N-(2-chlorophenyl)-N'-[4-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



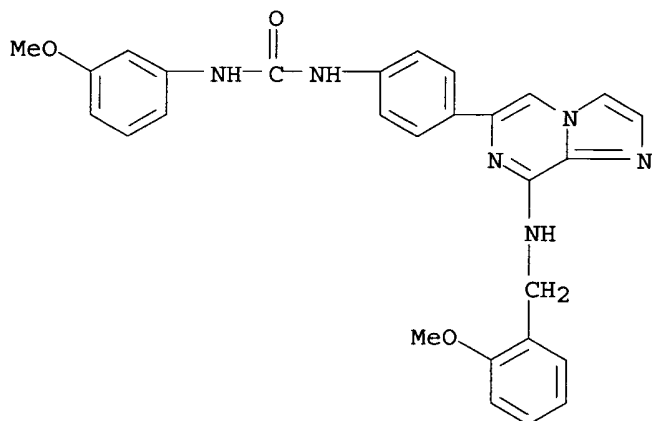
RN 618455-69-9 HCAPLUS

CN Urea, N-(2-methoxyphenyl)-N'-[4-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl] - (9CI) (CA INDEX NAME)



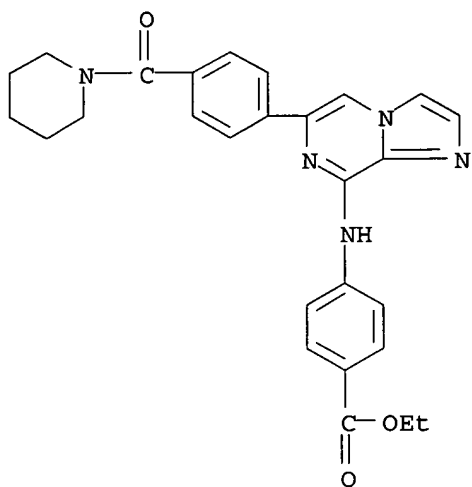
RN 618455-71-3 HCAPLUS

CN Urea, N-(3-methoxyphenyl)-N'-[4-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



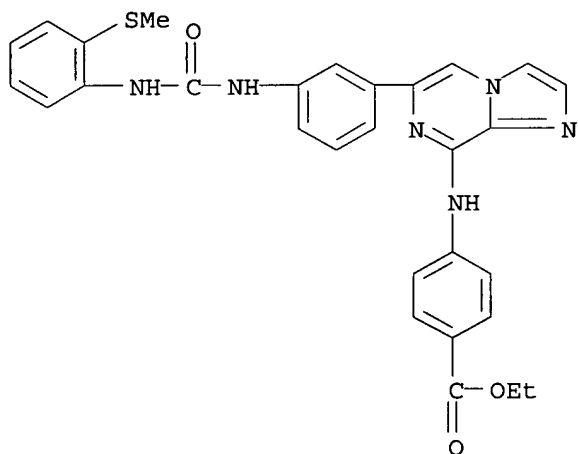
RN 618455-73-5 HCAPLUS

CN Benzoic acid, 4-[[6-[4-(1-piperidinylcarbonyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



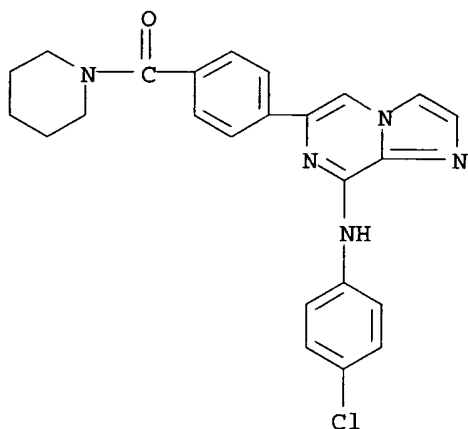
RN 618455-75-7 HCAPLUS

CN Benzoic acid, 4-[[6-[3-[[[2-(methylthio)phenyl]amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



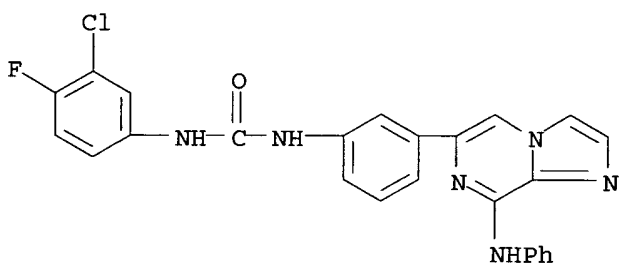
RN 618455-77-9 HCAPLUS

CN Piperidine, 1-[4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



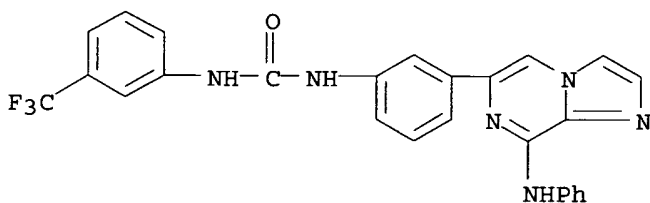
RN 618455-84-8 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



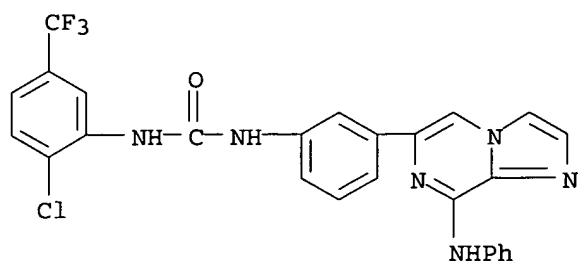
RN 618455-86-0 HCAPLUS

CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



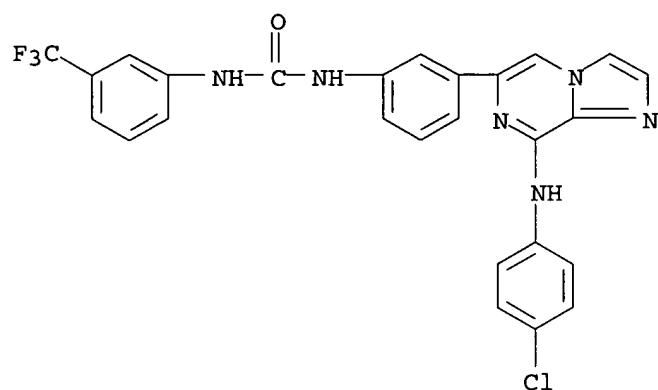
RN 618455-88-2 HCAPLUS

CN Urea, N-[2-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



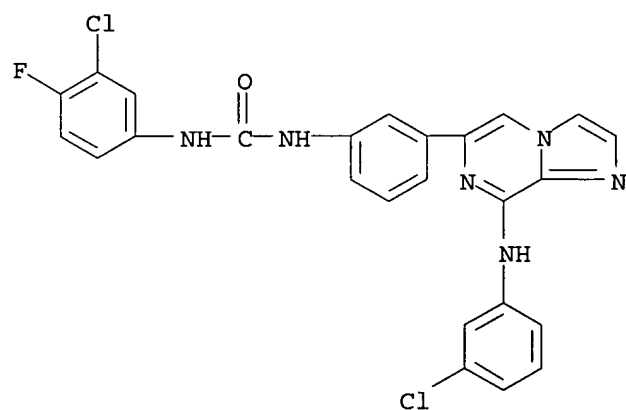
RN 618455-91-7 HCAPLUS

CN Urea, N-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



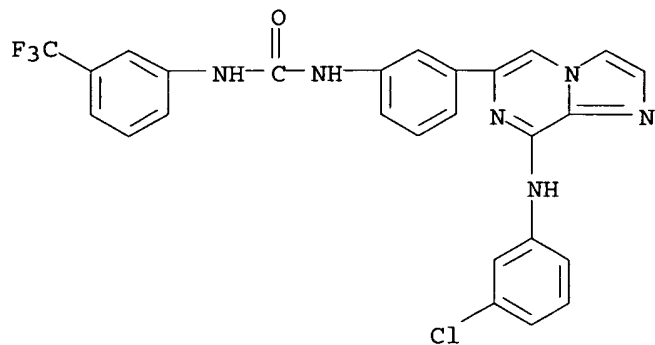
RN 618455-94-0 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



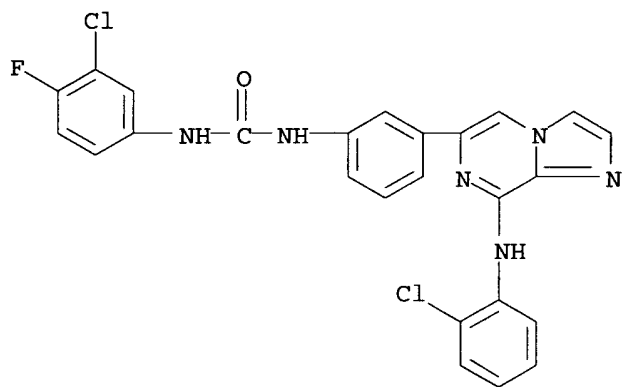
RN 618455-97-3 HCAPLUS

CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



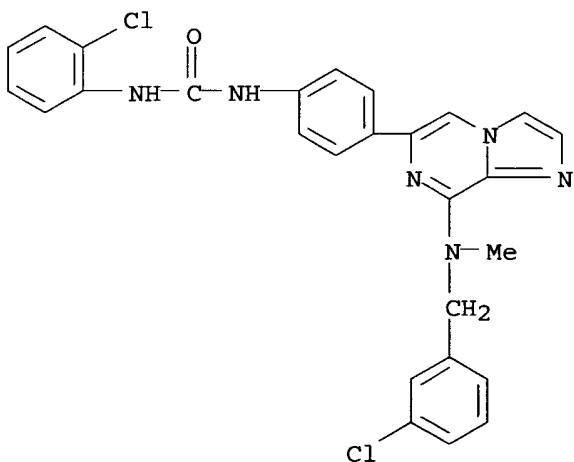
RN 618455-99-5 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



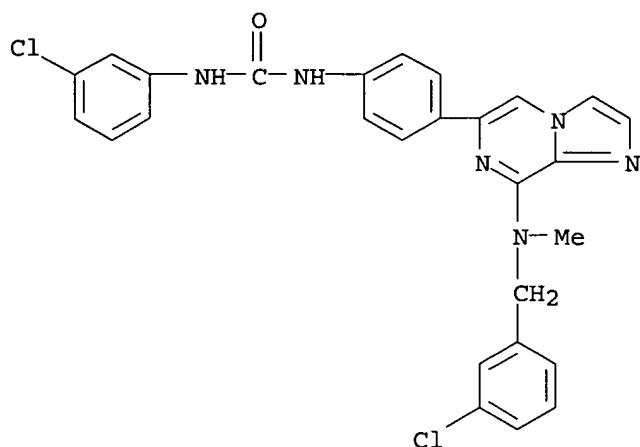
RN 673856-56-9 HCAPLUS

CN Urea, N-(2-chlorophenyl)-N'-[4-[8-[(3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



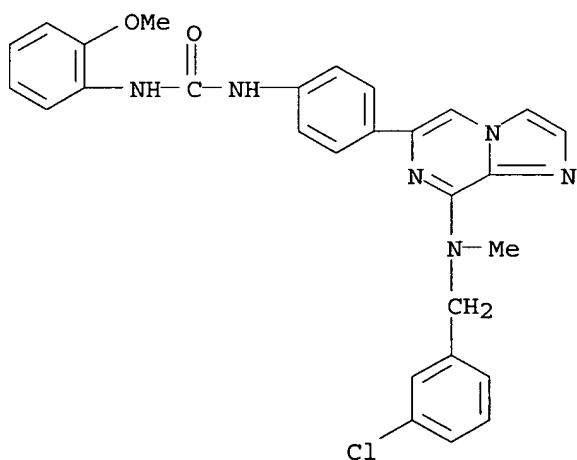
RN 673856-57-0 HCAPLUS

CN Urea, N-(3-chlorophenyl)-N'-[4-[8-[[3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



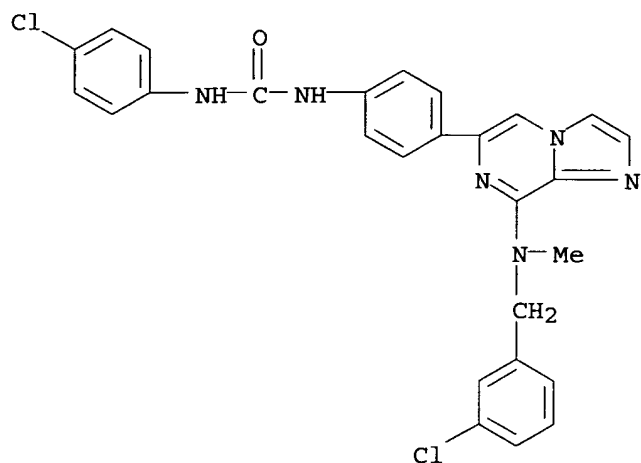
RN 673856-58-1 HCAPLUS

CN Urea, N-[4-[8-[[3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



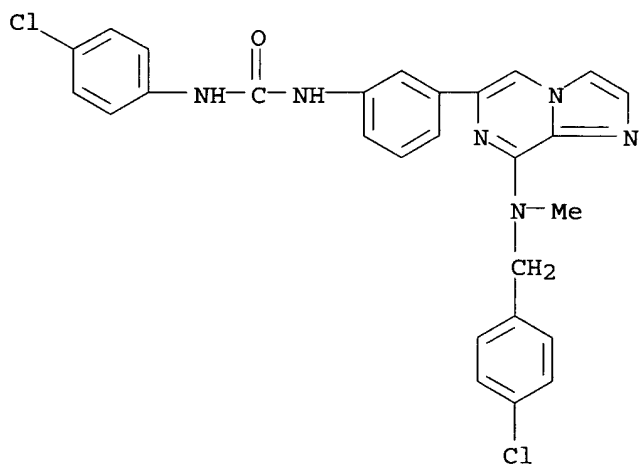
RN 673856-59-2 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[4-[8-[[3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



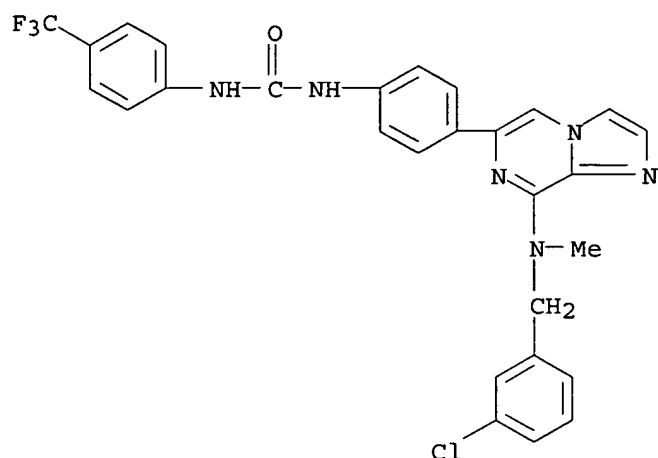
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CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



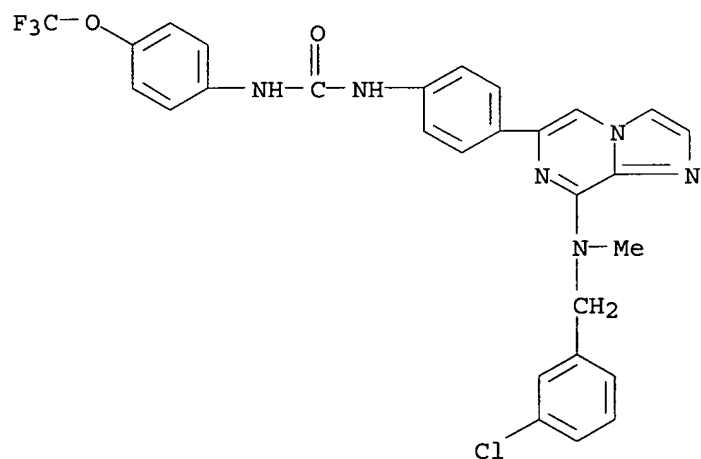
RN 673856-61-6 HCAPLUS

CN Urea, N-[4-[8-[[3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



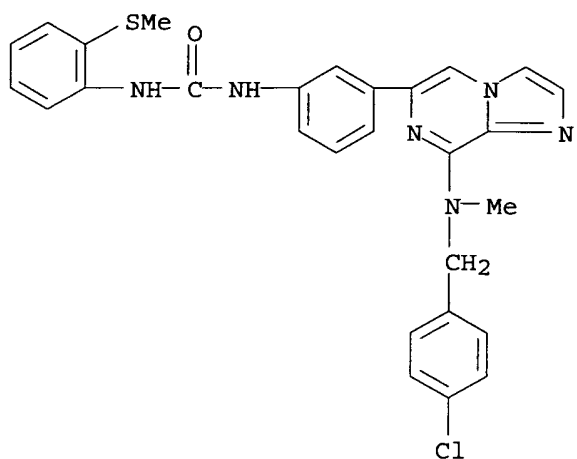
RN 673856-62-7 HCAPLUS

CN Urea, N-[4-[8-[[[(3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



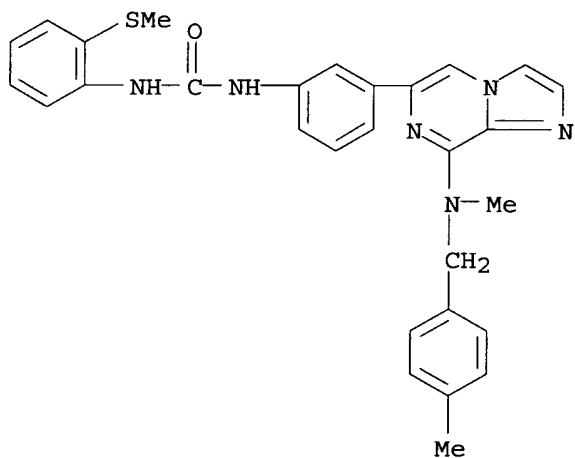
RN 673856-63-8 HCAPLUS

CN Urea, N-[3-[8-[[[(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



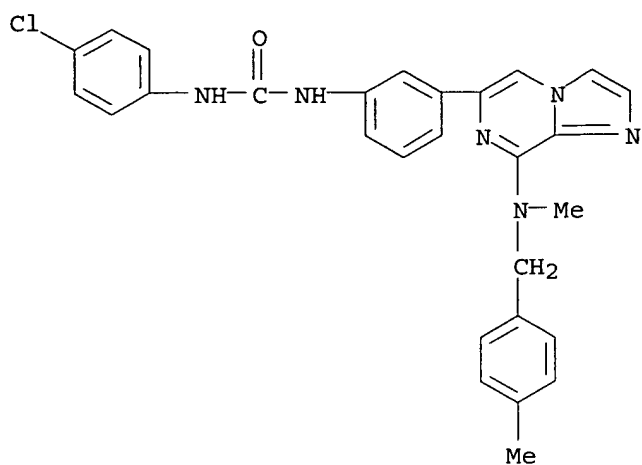
RN 673856-64-9 HCAPLUS

CN Urea, N-[3-[8-[methyl[(4-methylphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



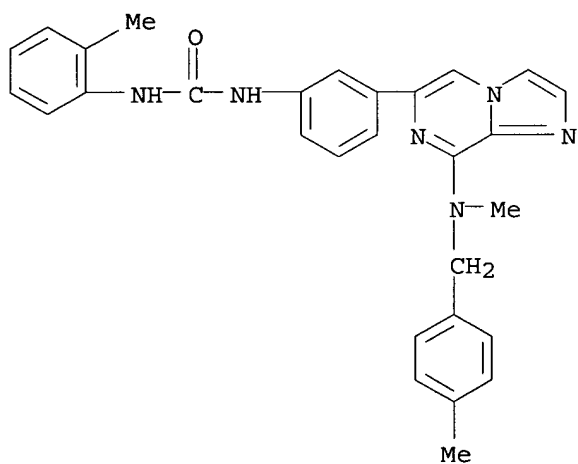
RN 673856-65-0 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[methyl[(4-methylphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



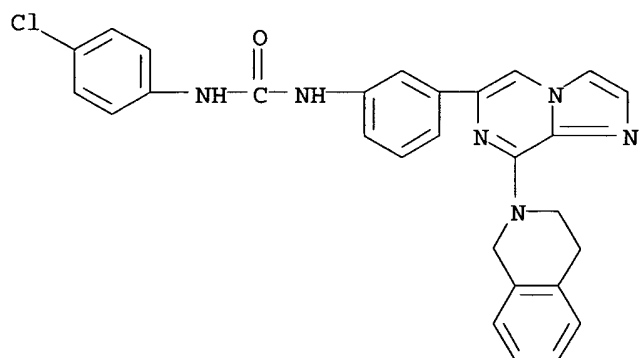
RN 673856-66-1 HCAPLUS

CN Urea, N-[3-[8-[methyl[(4-methylphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



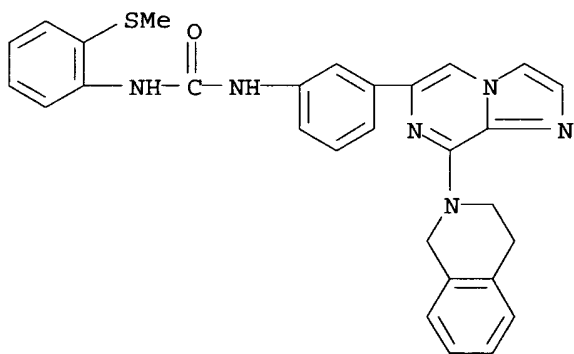
RN 673856-67-2 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-(3,4-dihydro-2(1H)-isoquinolinyl)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



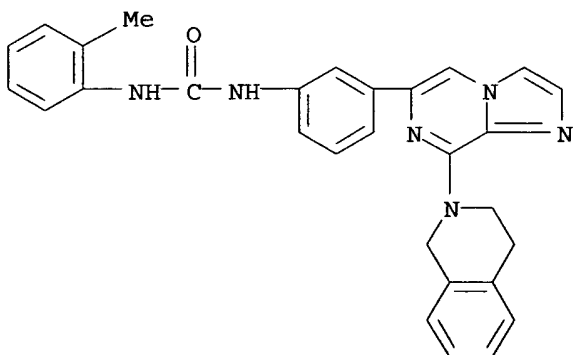
RN 673856-68-3 HCAPLUS

CN Urea, N-[3-[8-(3,4-dihydro-2(1H)-isoquinolinyl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



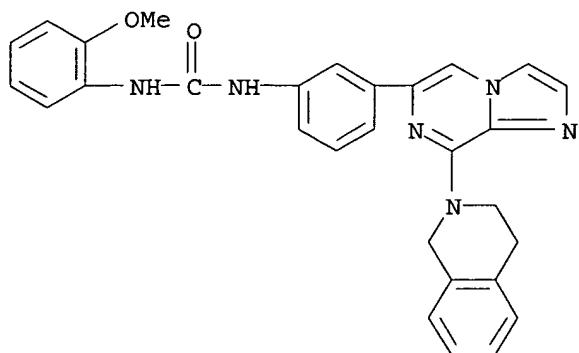
RN 673856-69-4 HCAPLUS

CN Urea, N-[3-[8-(3,4-dihydro-2(1H)-isoquinolinyl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



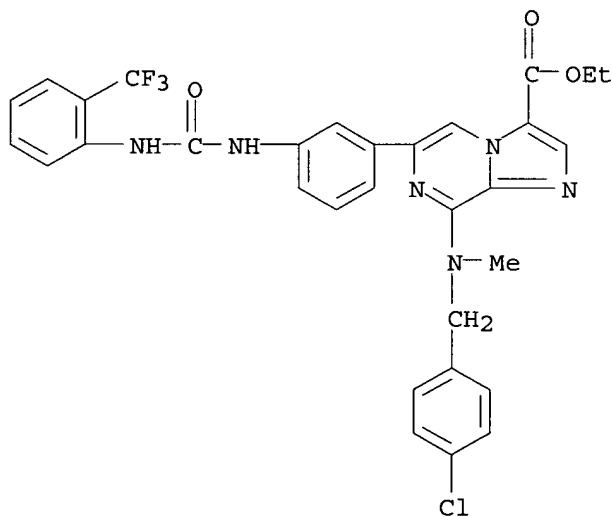
RN 673856-70-7 HCAPLUS

CN Urea, N-[3-[8-(3,4-dihydro-2(1H)-isoquinolinyl)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



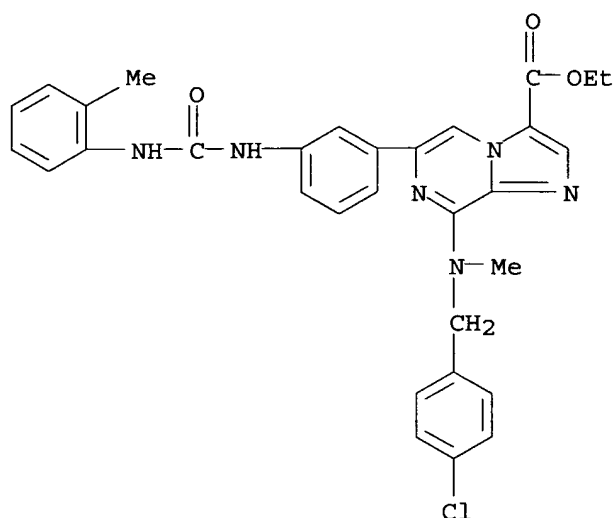
RN 673856-71-8 HCAPLUS

CN Imidazo[1,2-a]pyrazine-3-carboxylic acid, 8-[[[4-(2-methoxyphenyl)amino]carbonyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



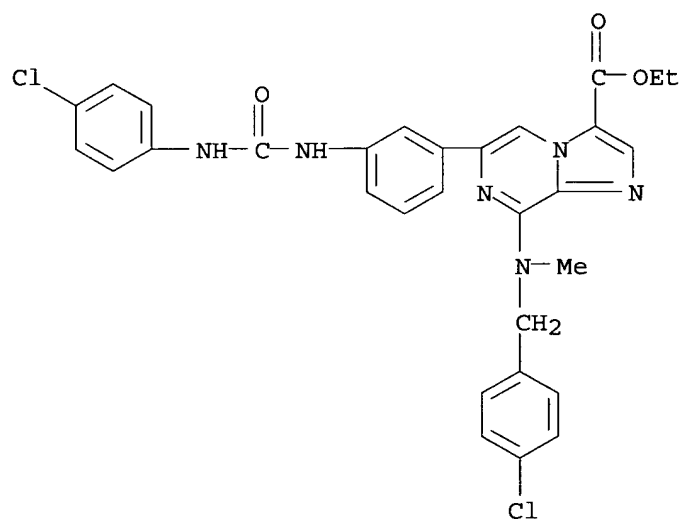
RN 673856-72-9 HCAPLUS

CN Imidazo[1,2-a]pyrazine-3-carboxylic acid, 8-[[[4-(2-methylphenyl)amino]carbonyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



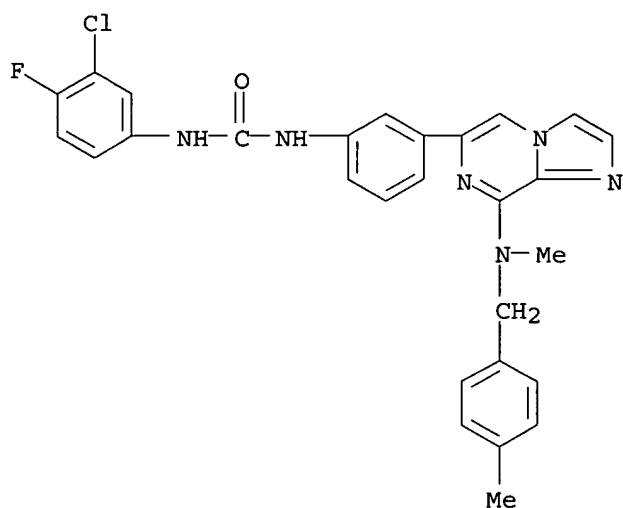
RN 673856-73-0 HCAPLUS

CN Imidazo[1,2-a]pyrazine-3-carboxylic acid, 6-[3-[[[(4-chlorophenyl)amino]carbonyl]amino]phenyl]-8-[[[(4-chlorophenyl)methyl]methylamino]-, ethyl ester (9CI) (CA INDEX NAME)



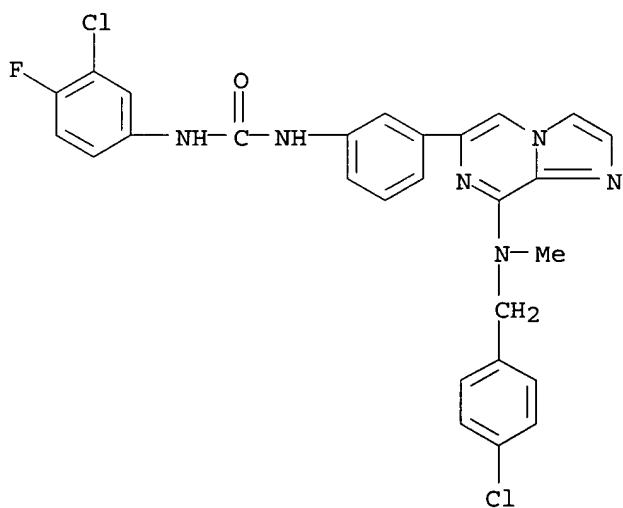
RN 673856-74-1 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[methyl[(4-methylphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



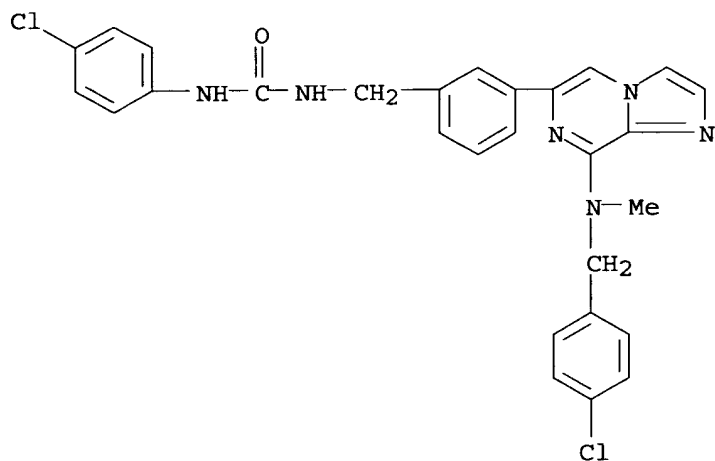
RN 673856-75-2 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



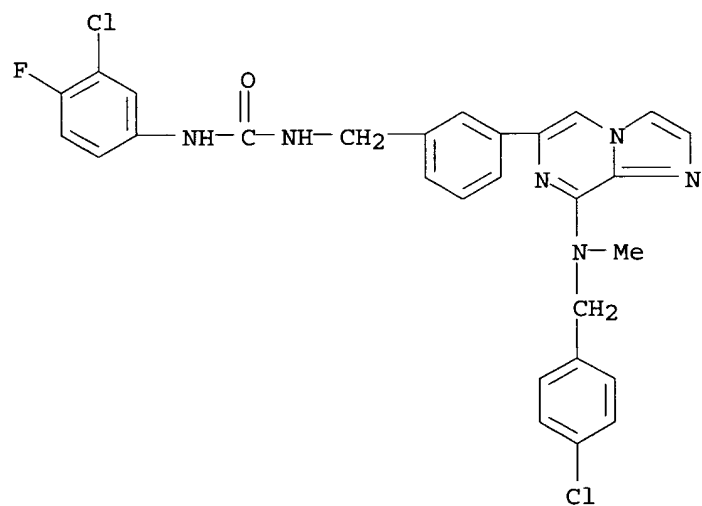
RN 673856-76-3 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)



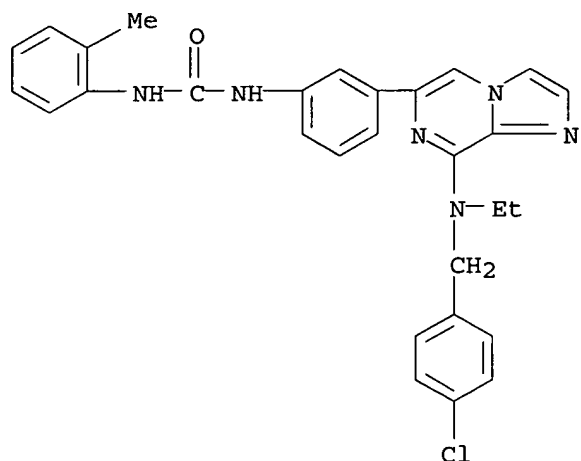
RN 673856-77-4 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)

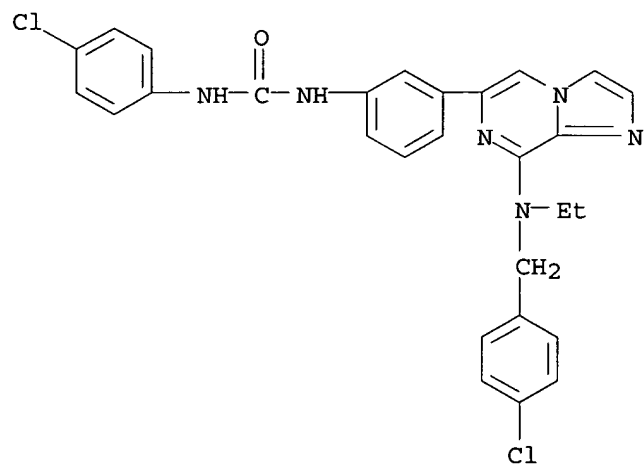


RN 673856-78-5 HCAPLUS

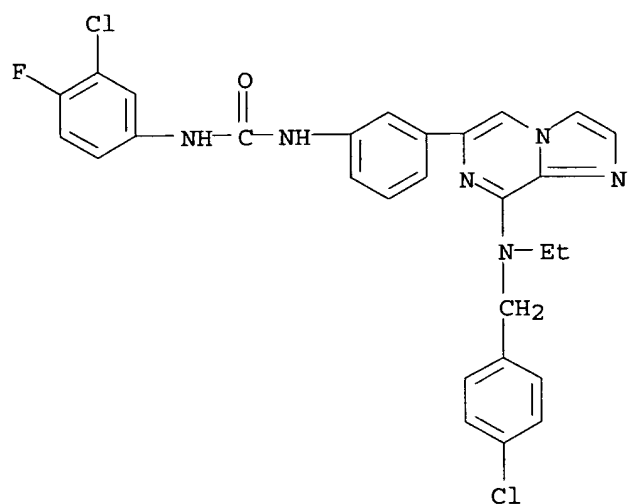
CN Urea, N-[3-[8-[[4-chlorophenyl)methyl]ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



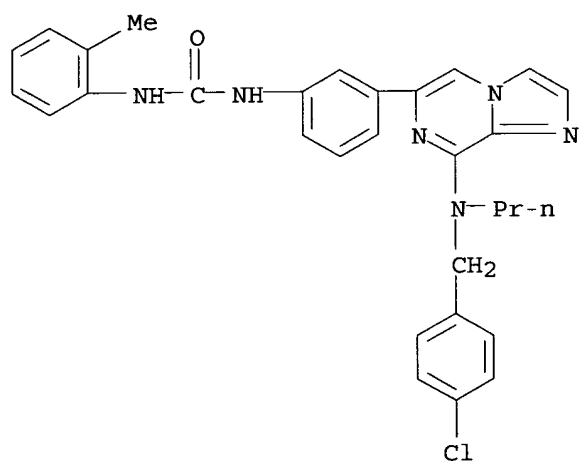
RN 673856-79-6 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl]ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



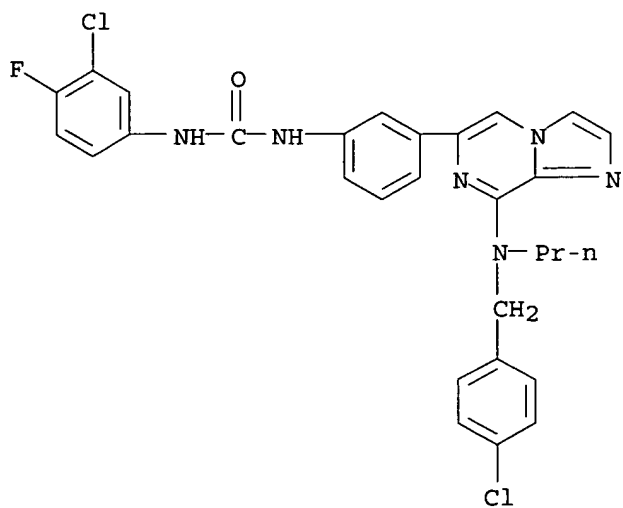
RN 673856-80-9 HCAPLUS
 CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl]ethylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 673856-81-0 HCAPLUS
 CN Urea, N-[3-[8-[[4-chlorophenyl)methyl]propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)

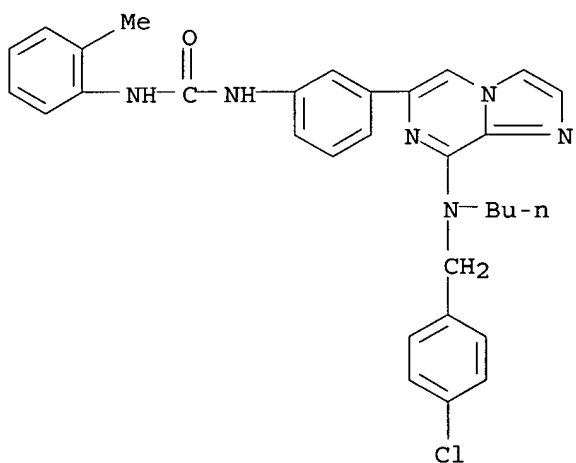


RN 673856-82-1 HCAPLUS
 CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl]propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



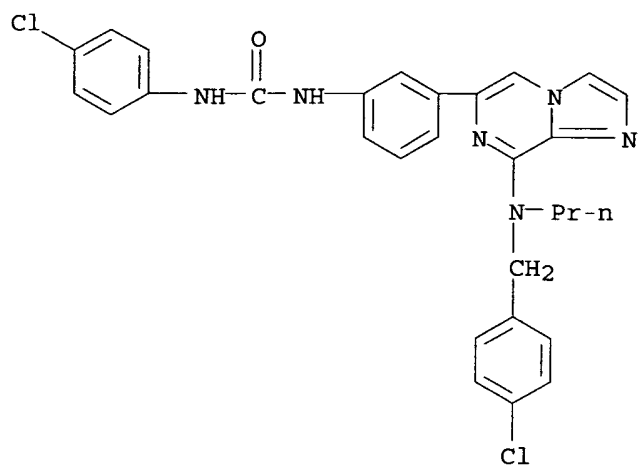
RN 673856-83-2 HCAPLUS

CN Urea, N-[3-[8-[butyl[(4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



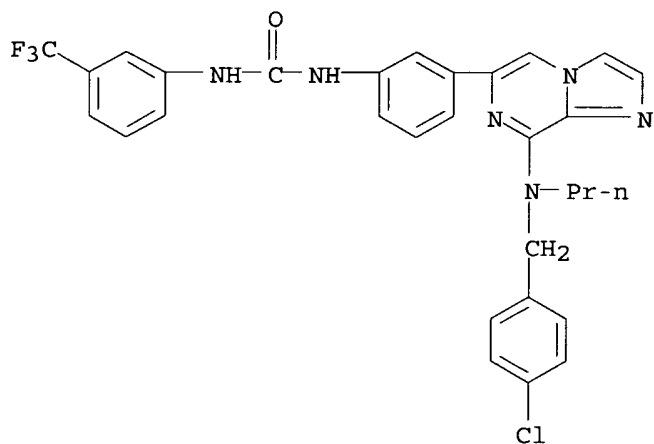
RN 673856-84-3 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[[(4-chlorophenyl)methyl]propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



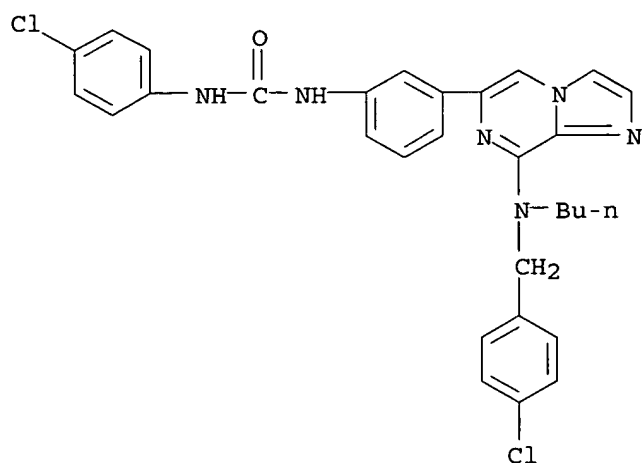
RN 673856-85-4 HCAPLUS

CN Urea, N-[3-[8-[[4-chlorophenyl)methyl]propylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



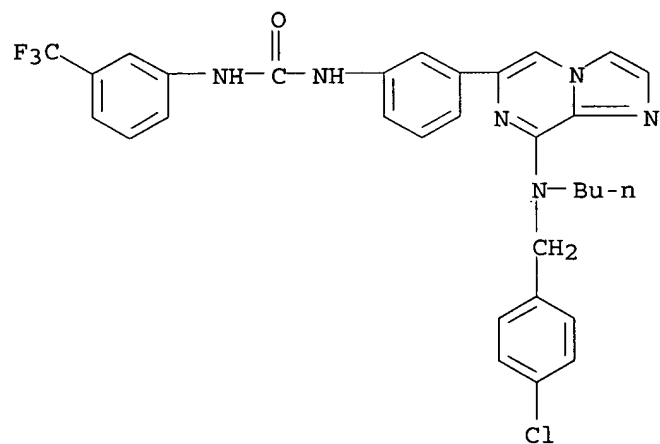
RN 673856-86-5 HCAPLUS

CN Urea, N-[3-[8-[butyl[(4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



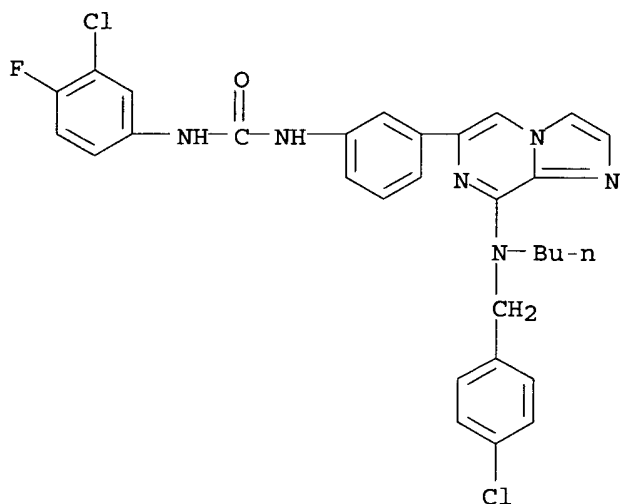
RN 673856-87-6 HCAPLUS

CN Urea, N-[3-[8-[butyl[(4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



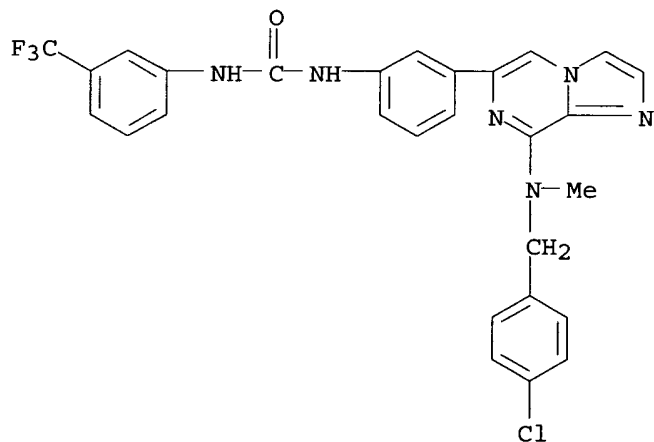
RN 673856-88-7 HCAPLUS

CN Urea, N-[3-[8-[butyl[(4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-chloro-4-fluorophenyl]- (9CI) (CA INDEX NAME)



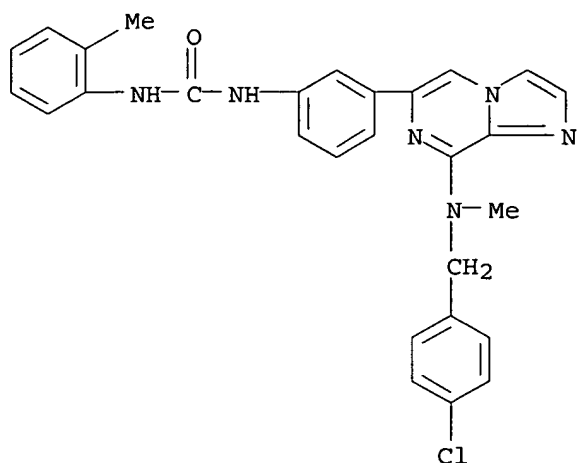
RN 673856-89-8 HCAPLUS

CN Urea, N-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



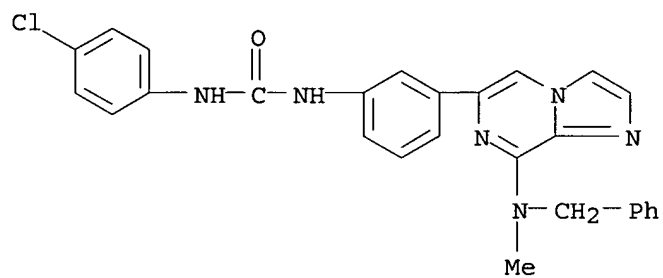
RN 673856-90-1 HCAPLUS

CN Urea, N-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



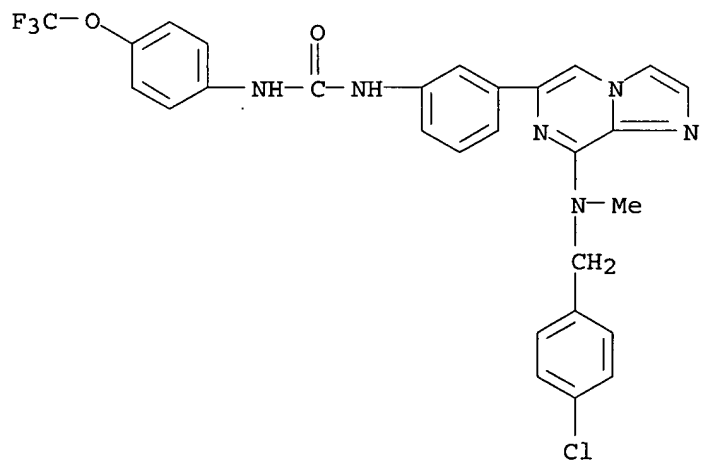
RN 673856-91-2 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[methyl(phenylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



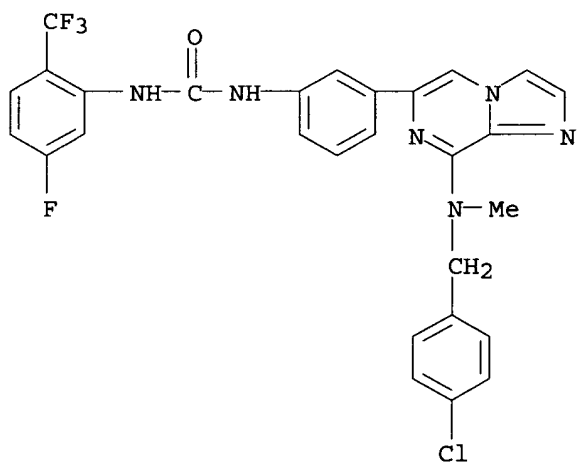
RN 673856-92-3 HCAPLUS

CN Urea, N-[3-[8-[[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



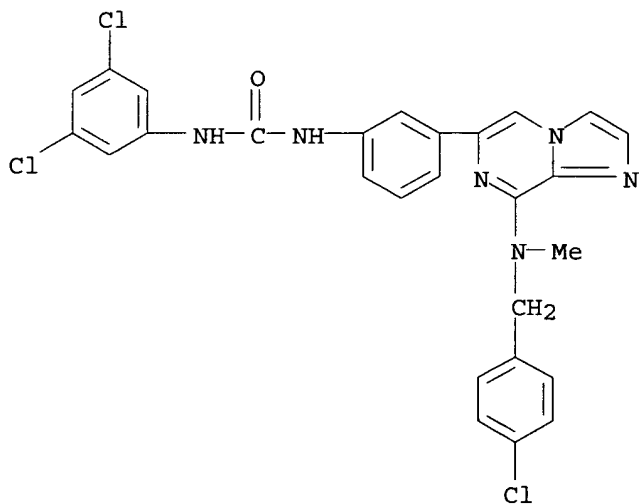
RN 673856-93-4 HCAPLUS

CN Urea, N-[3-[8-[[4-(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[5-fluoro-2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



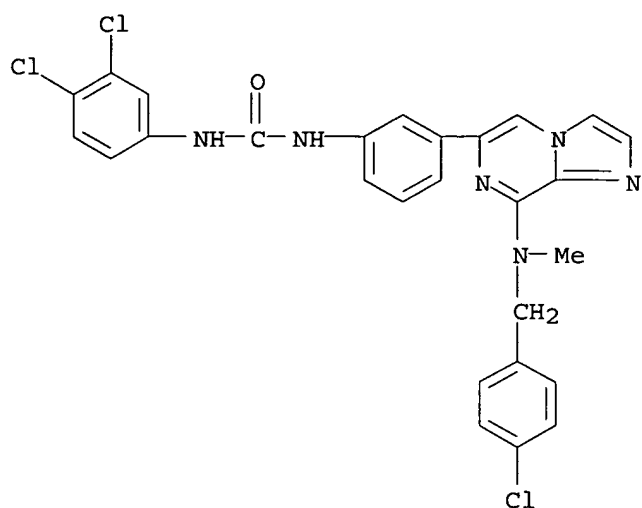
RN 673856-94-5 HCAPLUS

CN Urea, N-[3-[8-[[4-(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(3,5-dichlorophenyl)- (9CI) (CA INDEX NAME)



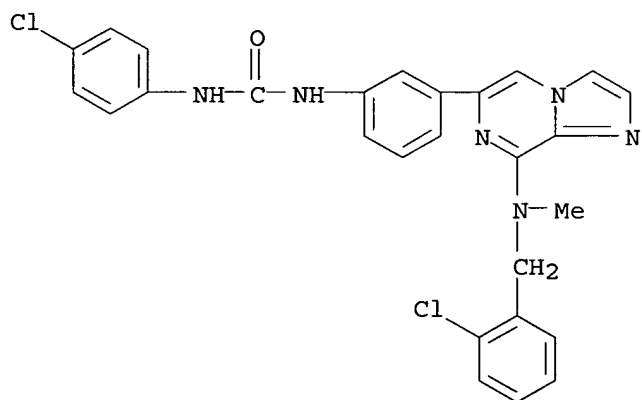
RN 673856-95-6 HCAPLUS

CN Urea, N-[3-[8-[[4-(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



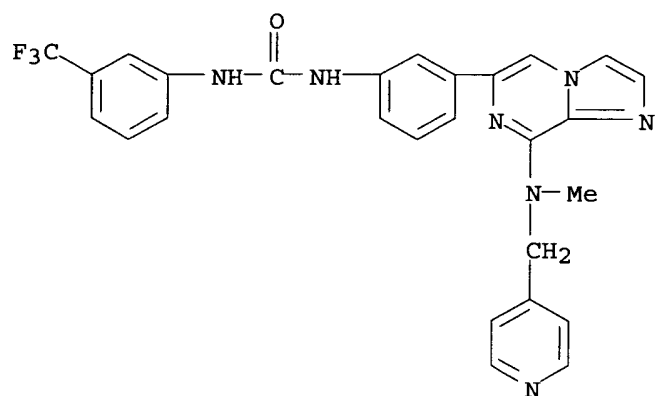
RN 673856-96-7 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[2-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



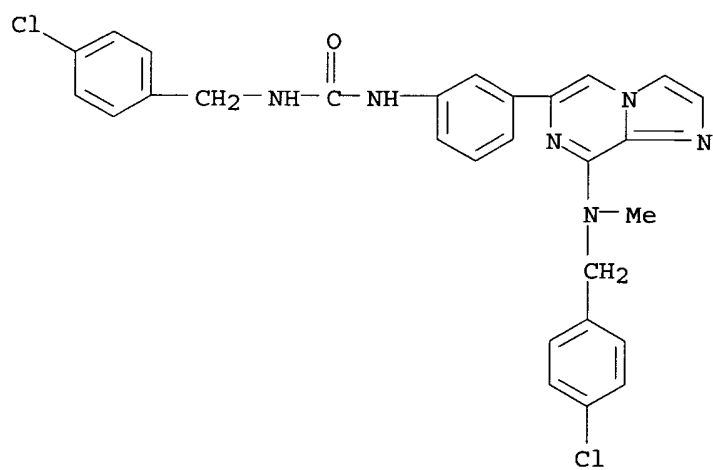
RN 673856-97-8 HCAPLUS

CN Urea, N-[3-[8-[methyl(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



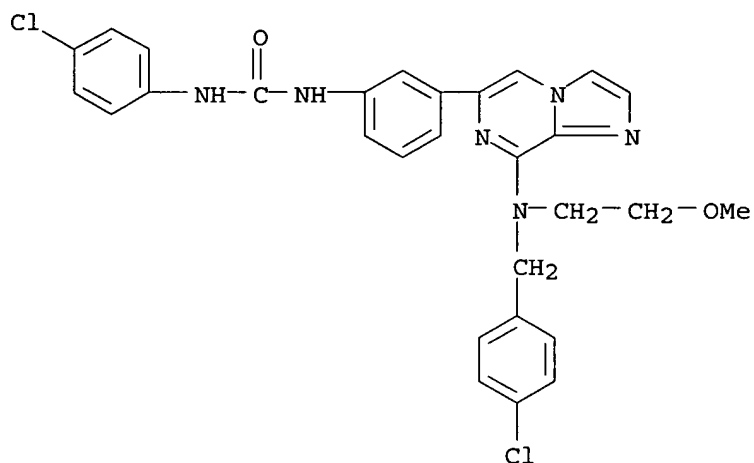
RN 673856-98-9 HCAPLUS

CN Urea, N-[(4-chlorophenyl)methyl]-N'-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
(CA INDEX NAME)



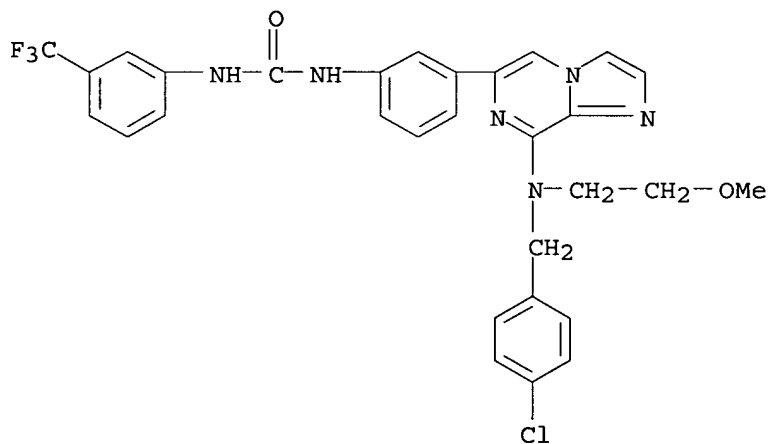
RN 673856-99-0 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[4-chlorophenyl)methyl] (2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



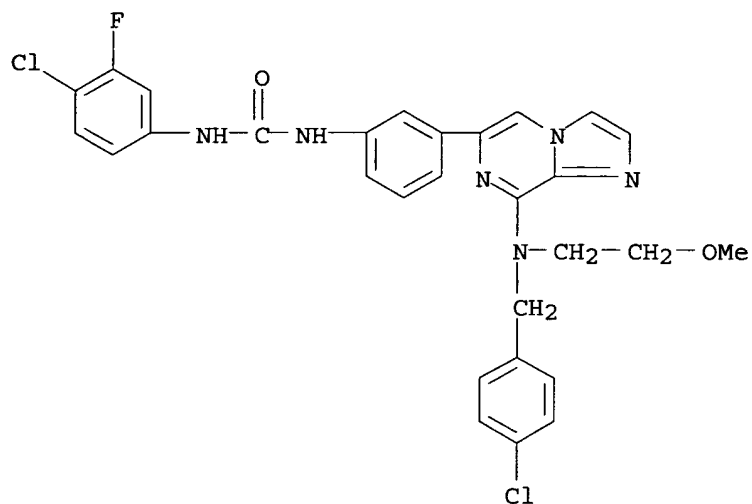
RN 673857-00-6 HCAPLUS

CN Urea, N-[3-[8-[[[4-chlorophenyl)methyl](2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

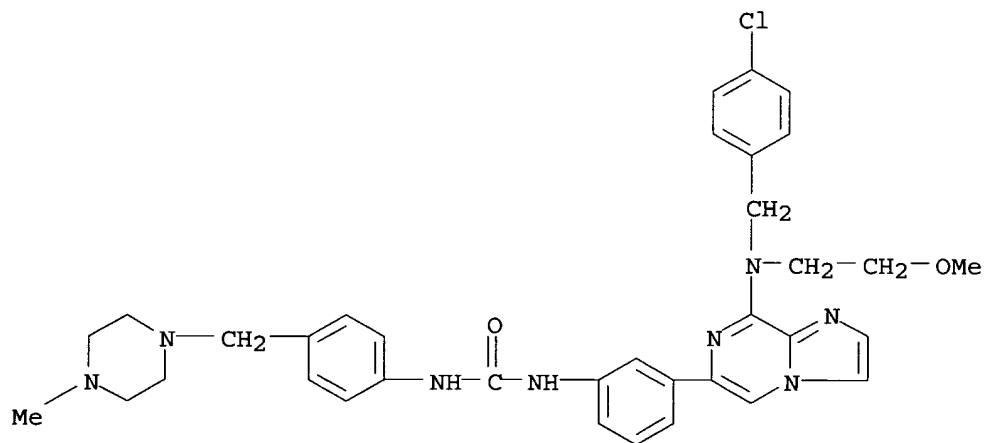


RN 673857-01-7 HCAPLUS

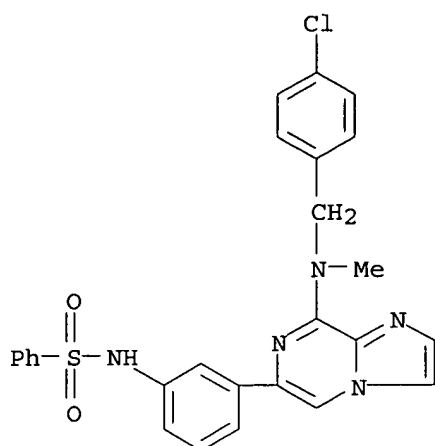
CN Urea, N-(4-chloro-3-fluorophenyl)-N'-[3-[8-[[[4-chlorophenyl)methyl](2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 673857-02-8 HCAPLUS
 CN Urea, N-[3-[8-[[(4-chlorophenyl)methyl] (2-methoxyethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-[(4-methyl-1-piperazinyl)methyl]phenyl]-
 (9CI) (CA INDEX NAME)

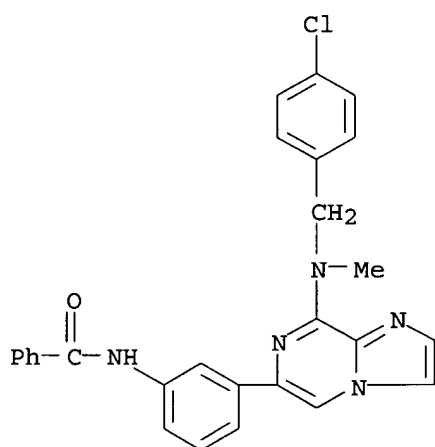


RN 673857-03-9 HCAPLUS
 CN Benzenesulfonamide, N-[3-[8-[[(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



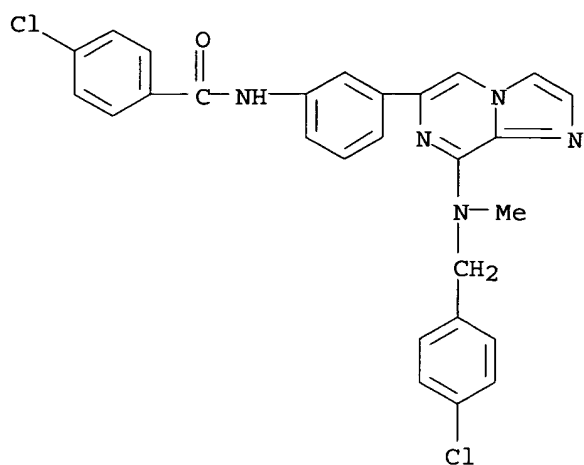
RN 673857-04-0 HCAPLUS

CN Benzamide, N-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



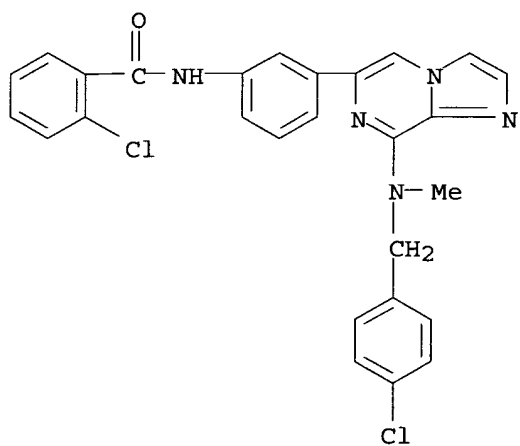
RN 673857-05-1 HCAPLUS

CN Benzamide, 4-chloro-N-[3-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



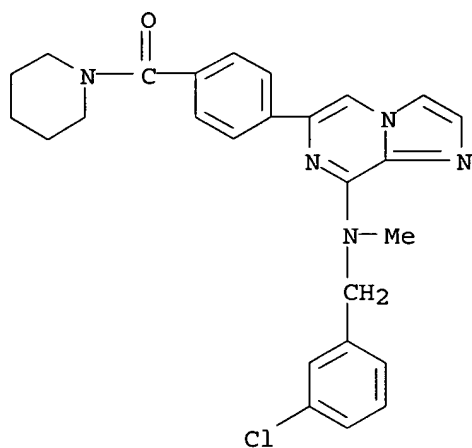
RN 673857-06-2 HCAPLUS

CN Benzamide, 2-chloro-N-[3-[8-[[4-(4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

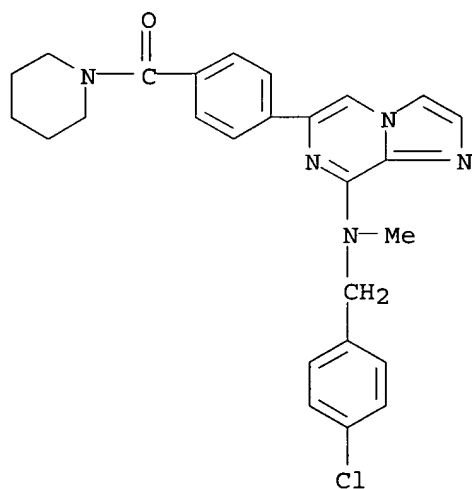


RN 673857-07-3 HCAPLUS

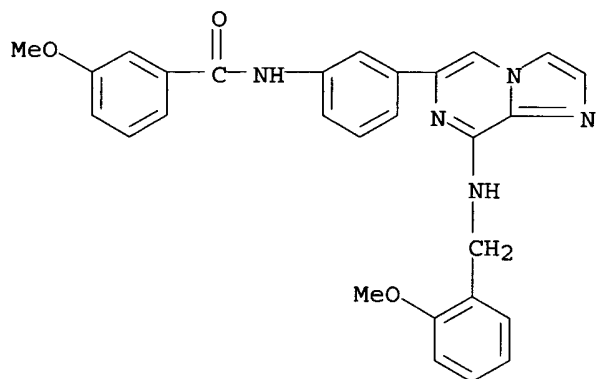
CN Piperidine, 1-[4-[8-[[3-(3-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



RN 673857-08-4 HCAPLUS
 CN Piperidine, 1-[4-[8-[[4-chlorophenyl)methyl]methylamino]imidazo[1,2-a]pyrazin-6-yl]benzoyl- (9CI) (CA INDEX NAME)

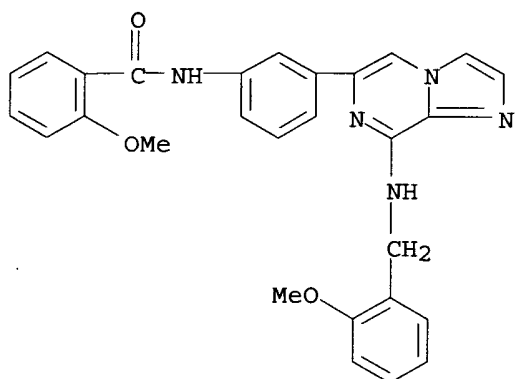


RN 673857-09-5 HCAPLUS
 CN Benzamide, 3-methoxy-N-[3-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl- (9CI) (CA INDEX NAME)



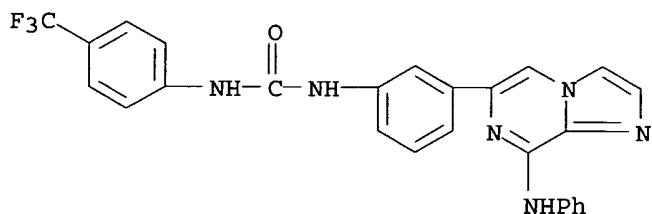
RN 673857-10-8 HCAPLUS

CN Benzamide, 2-methoxy-N-[3-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



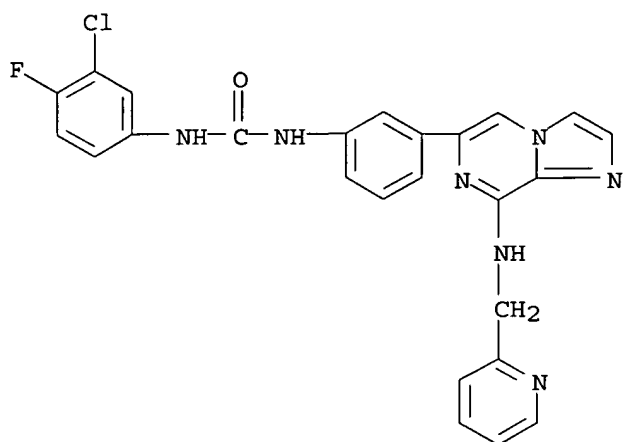
RN 673857-11-9 HCAPLUS

CN Urea, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

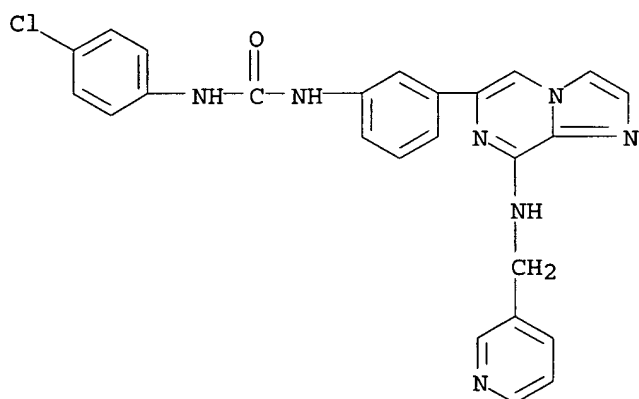


RN 673857-12-0 HCAPLUS

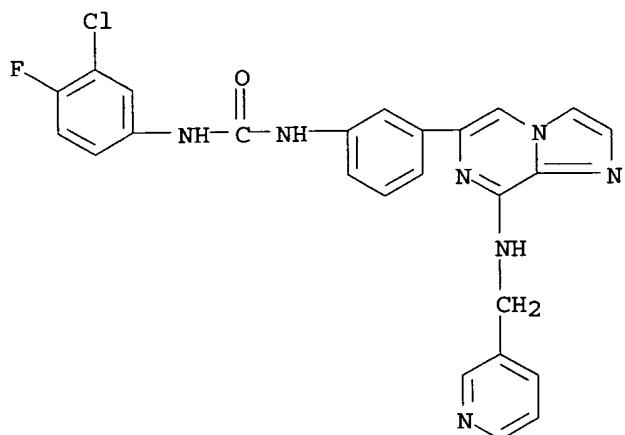
CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 673857-13-1 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

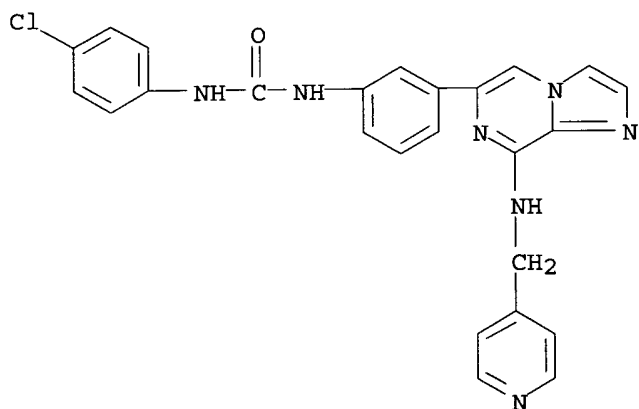


RN 673857-14-2 HCAPLUS
 CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(3-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



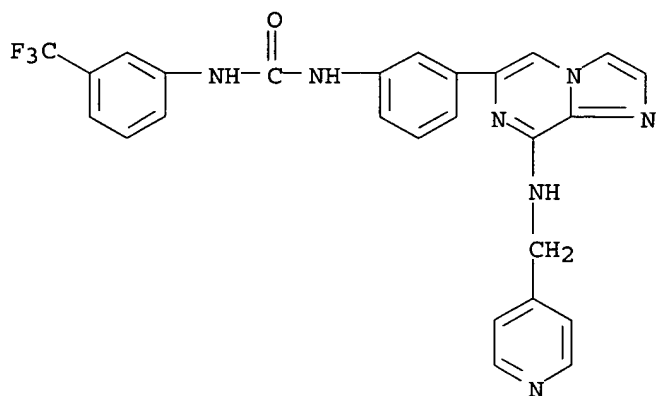
RN 673857-15-3 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



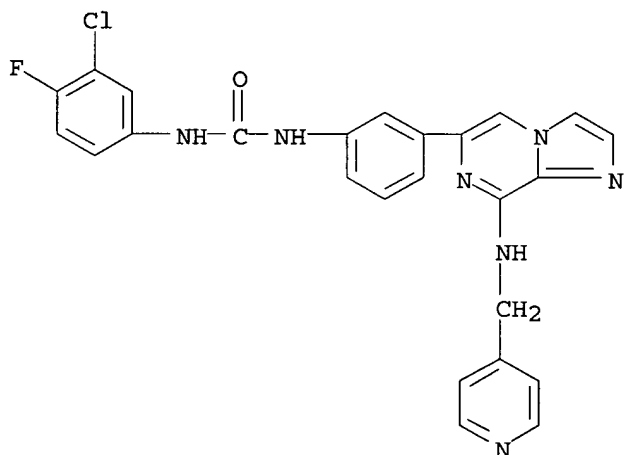
RN 673857-16-4 HCAPLUS

CN Urea, N-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(3-(trifluoromethyl)phenyl)- (9CI) (CA INDEX NAME)



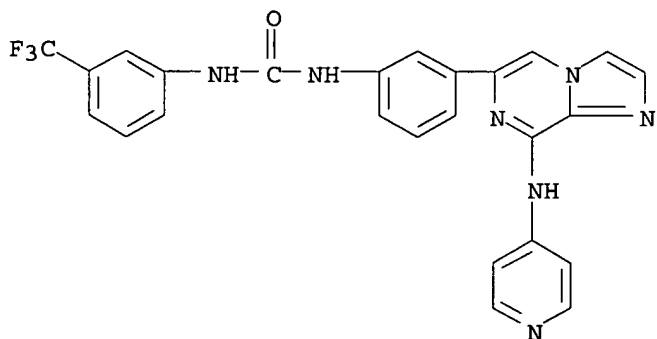
RN 673857-17-5 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(4-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



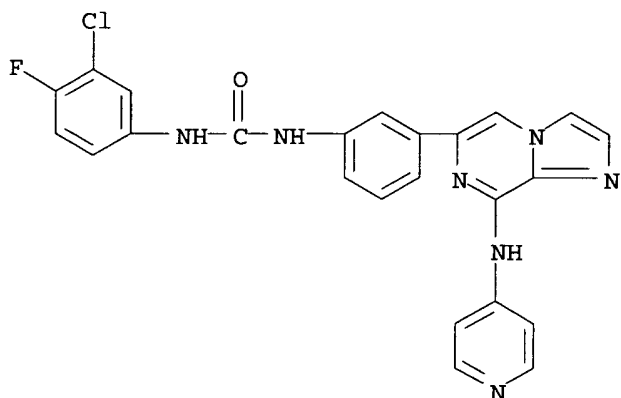
RN 673857-18-6 HCAPLUS

CN Urea, N-[3-[8-(4-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



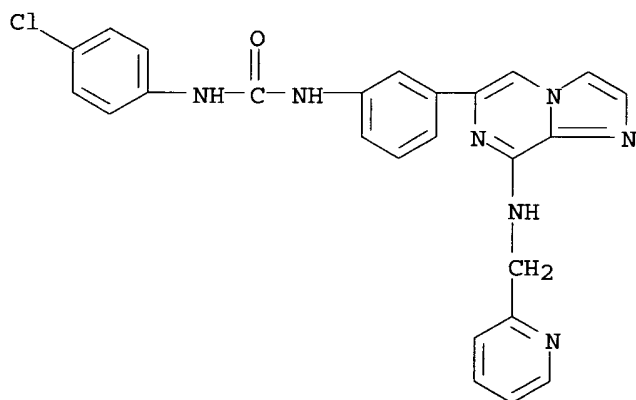
RN 673857-19-7 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-(4-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



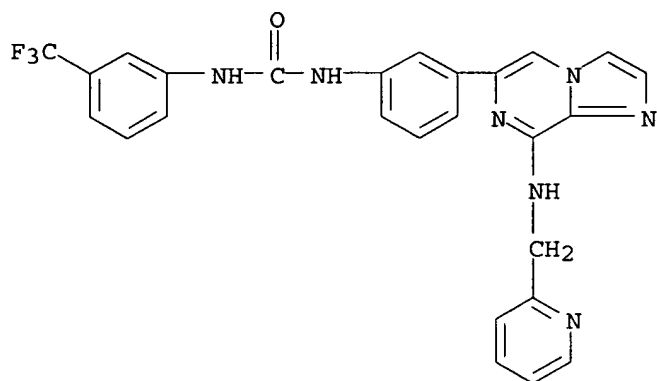
RN 673857-20-0 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



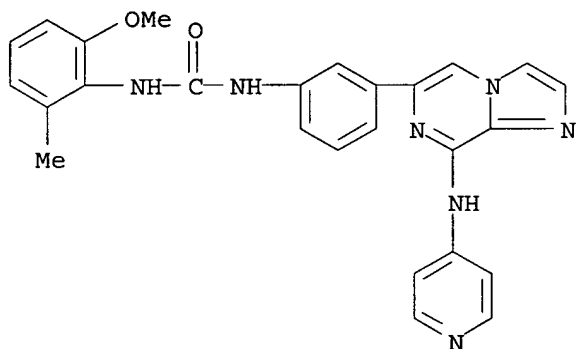
RN 673857-21-1 HCAPLUS

CN Urea, N-[3-[8-[(2-pyridinylmethyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



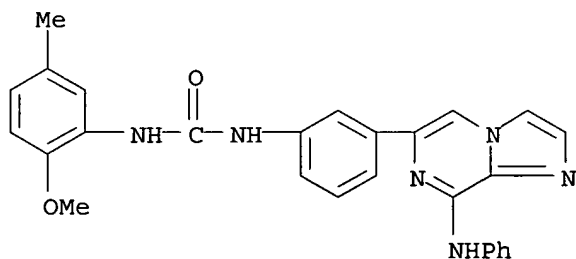
RN 673857-22-2 HCAPLUS

CN Urea, N-(2-methoxy-6-methylphenyl)-N'-[3-[8-(4-pyridinylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



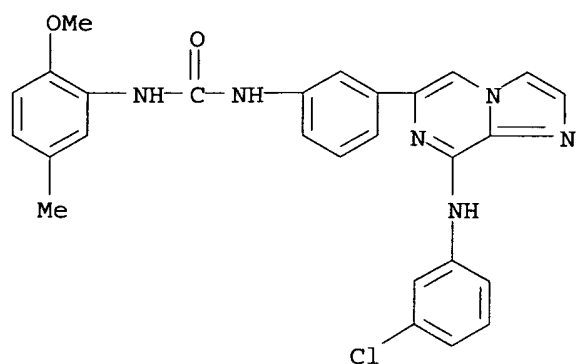
RN 673857-23-3 HCAPLUS

CN Urea, N-(2-methoxy-5-methylphenyl)-N'-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



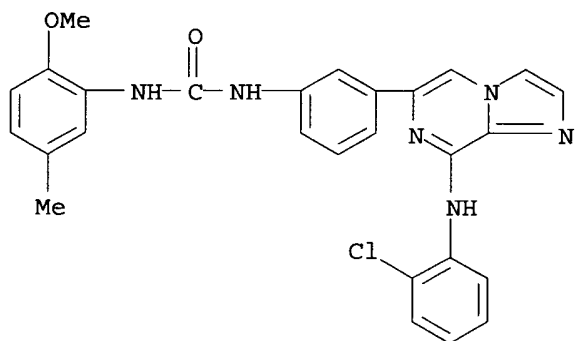
RN 673857-24-4 HCAPLUS

CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



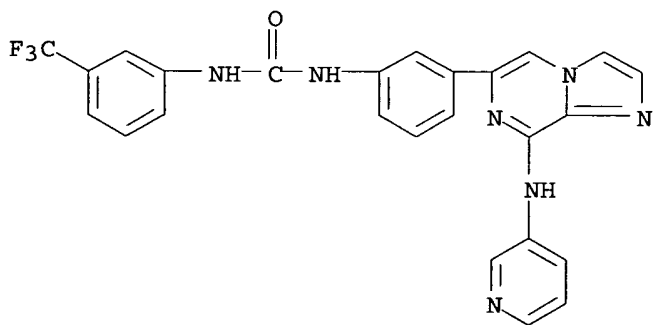
RN 673857-25-5 HCAPLUS

CN Urea, N-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-(2-methoxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



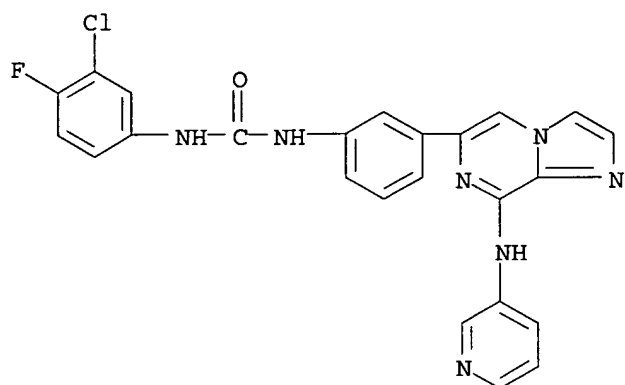
RN 673857-26-6 HCAPLUS

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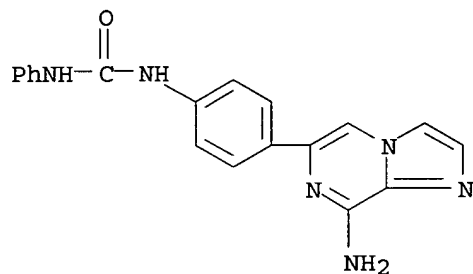


RN 673857-27-7 HCAPLUS

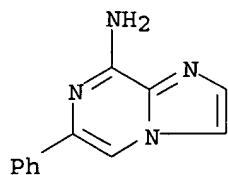
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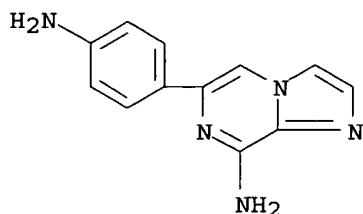
RN 673857-29-9 HCAPLUS
 CN Urea, N-[4-(8-aminoimidazo[1,2-a]pyrazin-6-yl)phenyl]-N'-phenyl- (9CI)
 (CA INDEX NAME)



IT 673857-28-8DP, 8-Amino-6-phenylimidazo[1,2-a]pyrazine, derivs.
 673857-30-2DP, 6-(4-Aminophenyl)imidazo[1,2-a]pyrazin-8-ylamine,
 derivs.
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (intermediate; preparation of arylimidazopyrazinylamines as kinase
 modulators)
 RN 673857-28-8 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl- (9CI) (CA INDEX NAME)



RN 673857-30-2 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(4-aminophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:855931 HCAPLUS

DOCUMENT NUMBER: 139:350757

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as AKT-1 kinase inhibitors

INVENTOR(S): Desimone, Robert Walter, Jr.; Pippin, Douglas A.; Darrow, James W.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

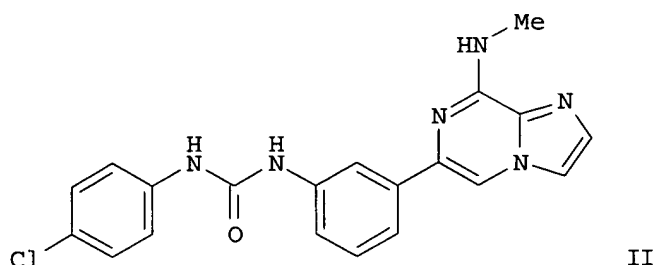
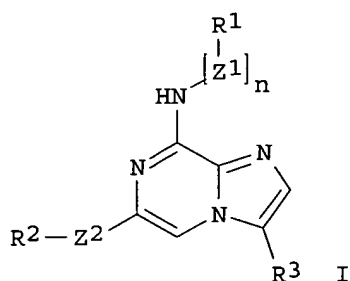
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2003089434 | A2 | 20031030 | WO 2003-US12222 | 20030421 |
| WO 2003089434 | A3 | 20040115 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2482991 | AA | 20031030 | CA 2003-2482991 | 20030421 |
| AU 2003221731 | A1 | 20031103 | AU 2003-221731 | 20030421 |
| US 2003212073 | A1 | 20031113 | US 2003-419682 | 20030421 |
| US 6919340 | B2 | 20050719 | | |
| BR 2003009398 | A | 20050201 | BR 2003-9398 | 20030421 |
| EP 1509526 | A2 | 20050302 | EP 2003-718470 | 20030421 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| JP 2005530739 | T2 | 20051013 | JP 2003-586154 | 20030421 |
| NO 2004004974 | A | 20041116 | NO 2004-4974 | 20041116 |
| PRIORITY APPLN. INFO.: | | | US 2002-374213P | P 20020419 |
| | | | WO 2003-US12222 | W 20030421 |
| OTHER SOURCE(S): | MARPAT 139:350757 | | | |
| GI | | | | |



AB The title compds. [I; R1 = H, cycloalkylmethyl, alkyl, etc.; R2 = alkyl, cycloalkylmethyl, alkoxy, etc.; R3 = H, alkyl, etc.; Z1 = CO, (un)substituted (CH2)m, CONH, NHSO2, SO2NH; n = 0-1; m = 0-2; Z2 = phenylene, naphthylene, CO, etc.] which are of particular utility in the treatment of kinase-implicated disorders, were prepared. General methods of preparation were given. All exemplified compds. I such as II were tested in standard AKT-1 kinase assay and standard assay to evaluate modulation of cell growth in soft agar (using cell lines HCT-15, MiaPaca2, MCF-7 and NIH3T3 clone stably overexpressing transfected myrAkt-1 human gene), and exhibited IC50 of $\leq 25 \mu\text{M}$. Pharmaceutical composition comprising the compound I is claimed.

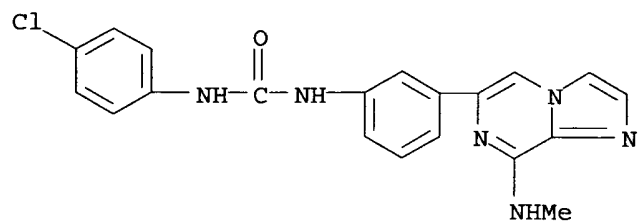
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 618454-91-4P 618454-95-8P 618455-01-9P
 618455-08-6P 618455-13-3P 618455-19-9P
 618455-25-7P 618455-30-4P 618455-36-0P
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 618455-54-2P 618455-57-5P 618455-60-0P
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 618455-91-7P 618455-94-0P 618455-97-3P
 618455-99-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazo[1,2-a]pyrazin-8-ylamines as AKT-1 kinase inhibitors)

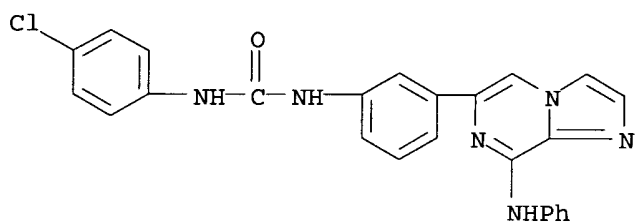
RN 618454-74-3 HCAPLUS

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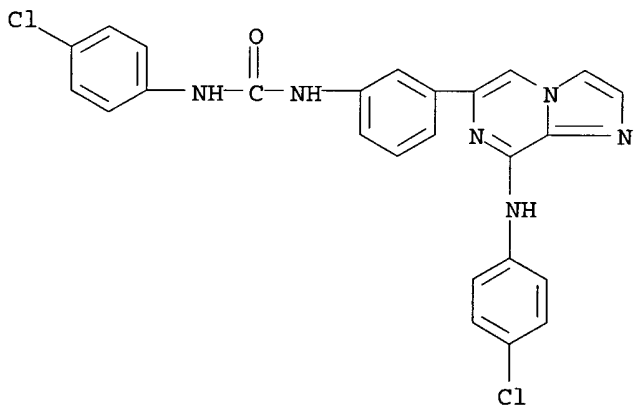
RN 618454-80-1 HCAPLUS

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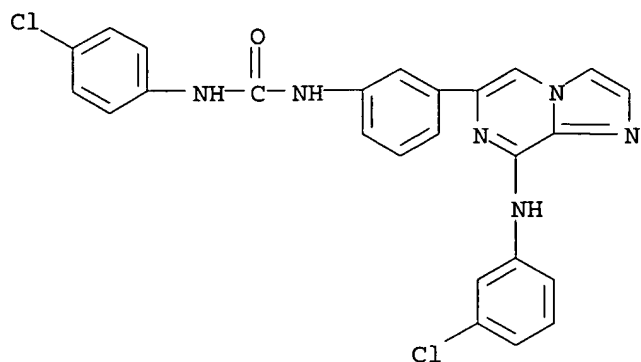
RN 618454-86-7 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

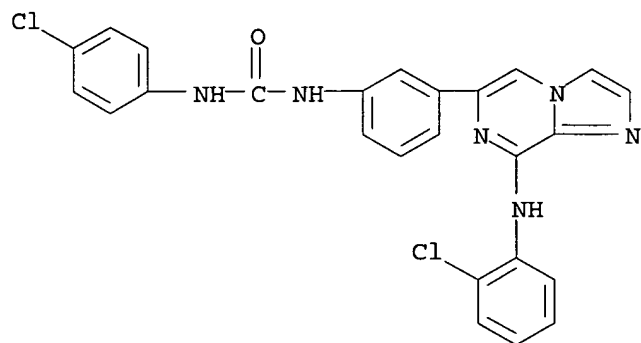


RN 618454-91-4 HCAPLUS

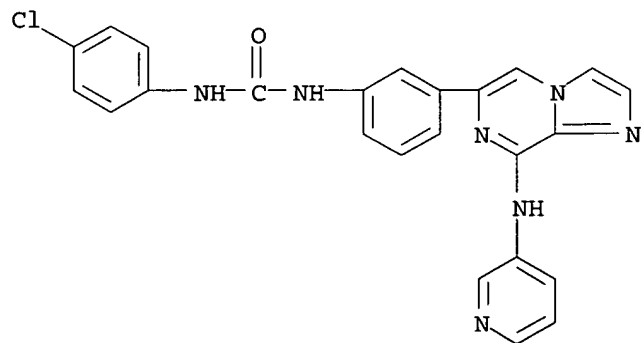
CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



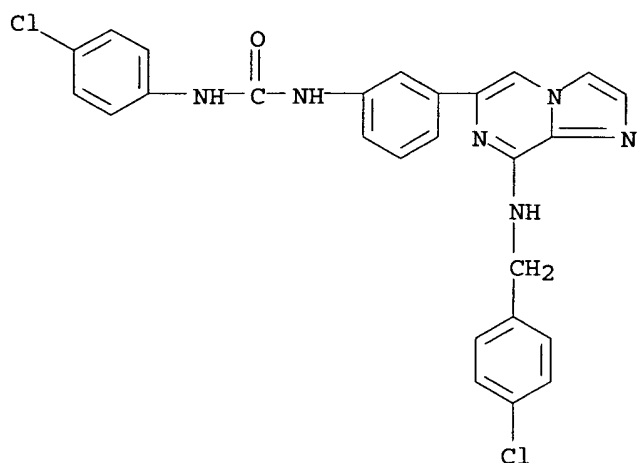
RN 618454-95-8 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-01-9 HCAPLUS
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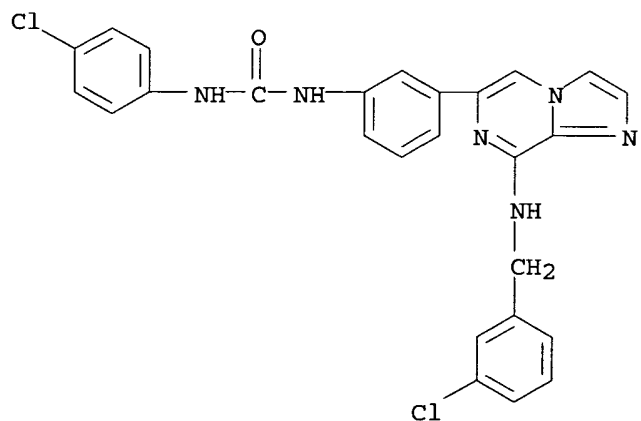


RN 618455-08-6 HCAPLUS
 CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[4-(4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



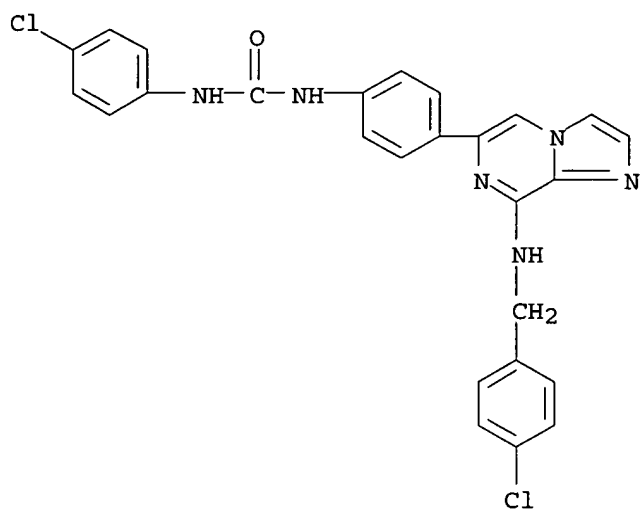
RN 618455-13-3 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[3-[8-[[3-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



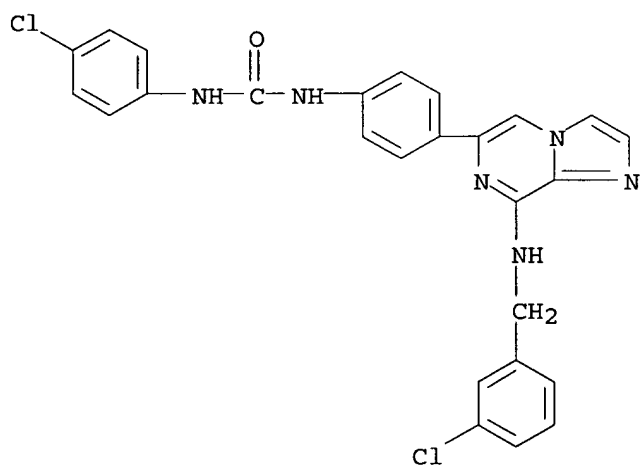
RN 618455-19-9 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[4-[8-[[4-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



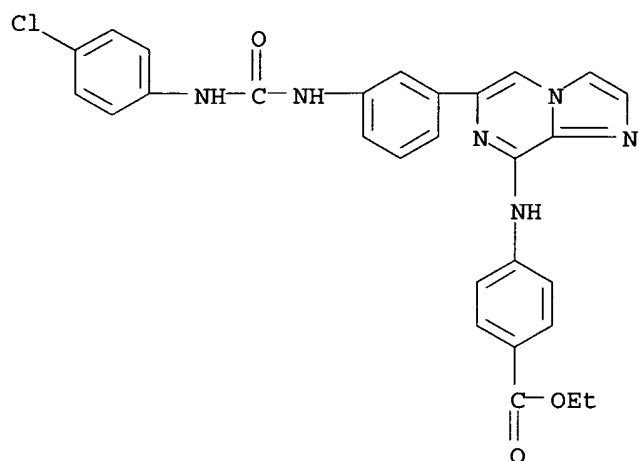
RN 618455-25-7 HCAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[4-[8-[[3-chlorophenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

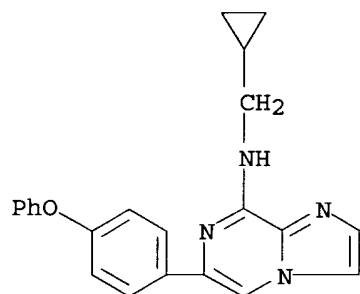


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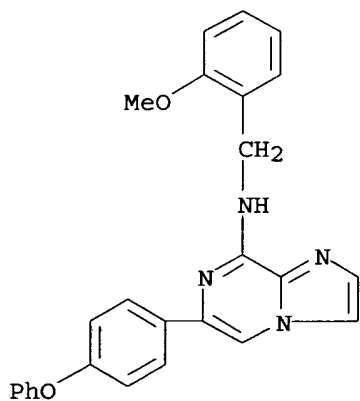
CN Benzoic acid, 4-[[6-[3-[[[4-chlorophenyl)amino]carbonyl]amino]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 618455-36-0 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-(cyclopropylmethyl)-6-(4-phenoxyphenyl)-
 (9CI) (CA INDEX NAME)

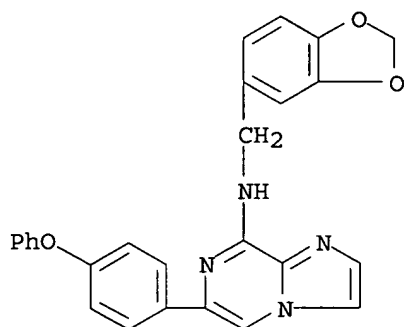


RN 618455-41-7 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-[(2-methoxyphenyl)methyl]-6-(4-
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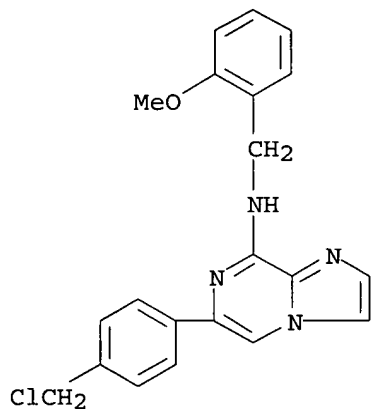
RN 618455-47-3 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-(1,3-benzodioxol-5-ylmethyl)-6-(4-

phenoxyphenyl) - (9CI) (CA INDEX NAME)



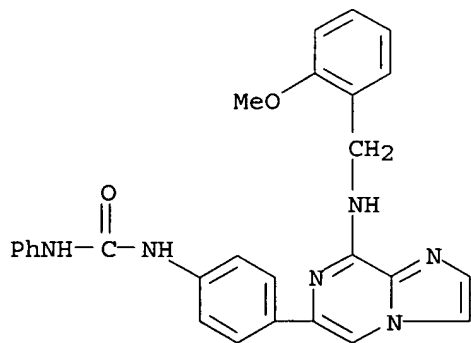
RN 618455-50-8 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[4-(chloromethyl)phenyl]-N-[(2-methoxyphenyl)methyl] - (9CI) (CA INDEX NAME)



RN 618455-54-2 HCAPLUS

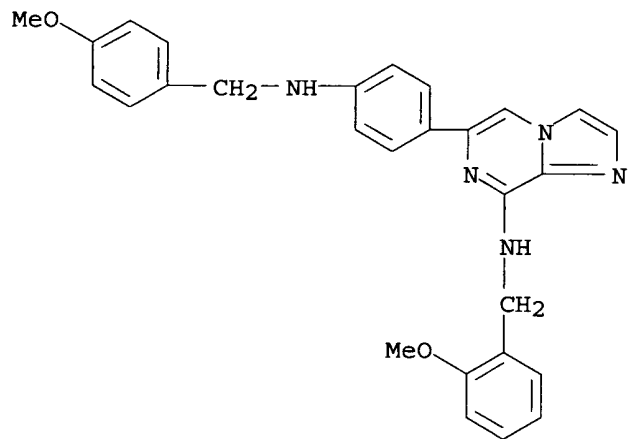
CN Urea, N-[4-[8-[[[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-phenyl- (9CI) (CA INDEX NAME)



RN 618455-57-5 HCAPLUS

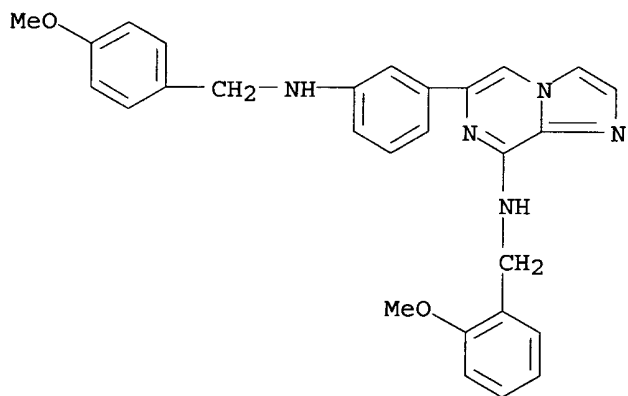
CN Imidazo[1,2-a]pyrazin-8-amine, N-[(2-methoxyphenyl)methyl]-6-[4-[[4-

methoxyphenyl)methyl]aminolphenyl]- (9CI) (CA INDEX NAME)



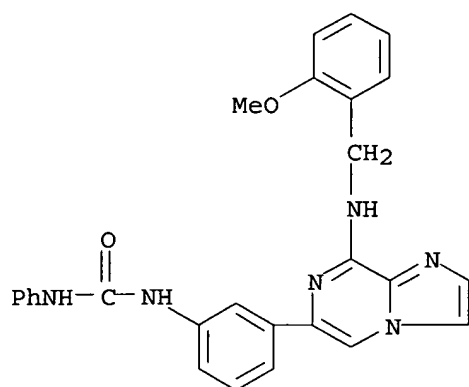
RN 618455-60-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[(2-methoxyphenyl)methyl]-6-[3-[(4-methoxyphenyl)methyl]aminolphenyl]- (9CI) (CA INDEX NAME)



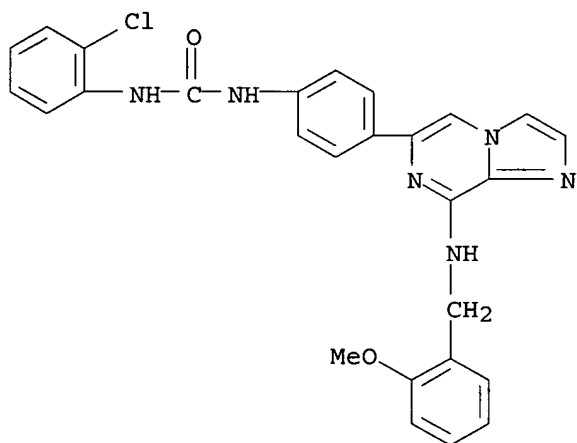
RN 618455-63-3 HCAPLUS

CN Urea, N-[3-[8-[[[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-phenyl]- (9CI) (CA INDEX NAME)



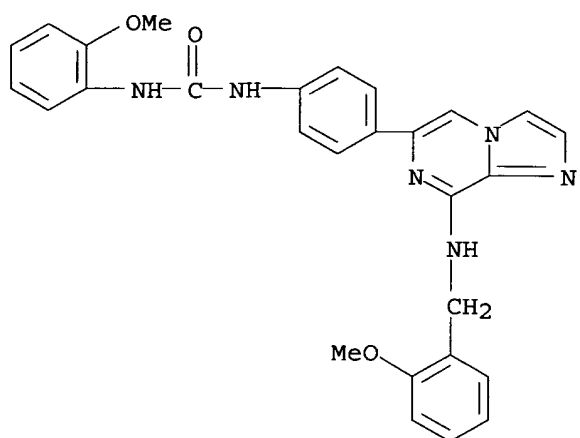
RN 618455-66-6 HCAPLUS

CN Urea, N-(2-chlorophenyl)-N'-[4-[8-[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



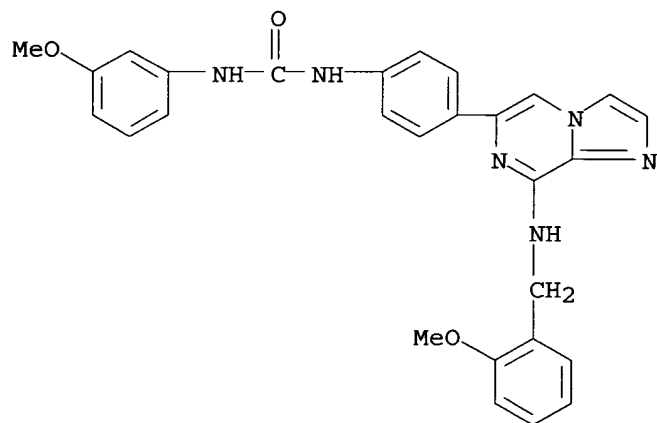
RN 618455-69-9 HCAPLUS

CN Urea, N-(2-methoxyphenyl)-N'-[4-[8-[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



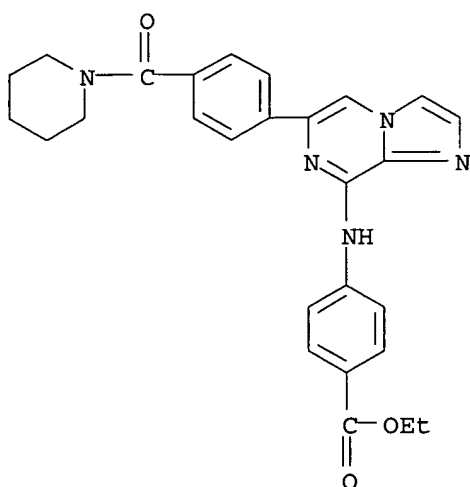
RN 618455-71-3 HCAPLUS

CN Urea, N-(3-methoxyphenyl)-N'-[4-[8-[[2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



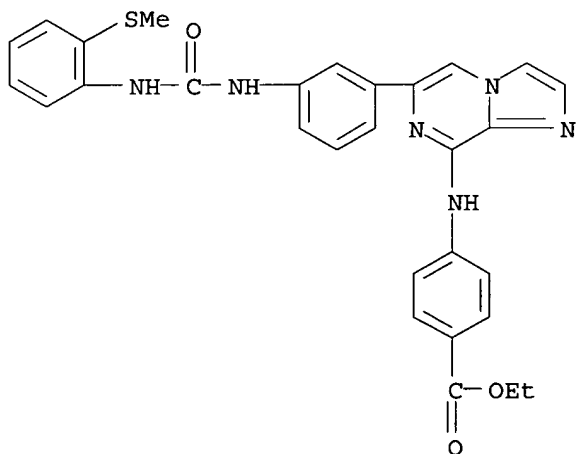
RN 618455-73-5 HCAPLUS

CN Benzoic acid, 4-[[6-[4-(1-piperidinylcarbonyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



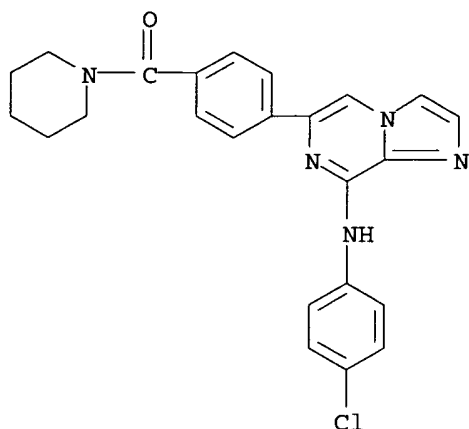
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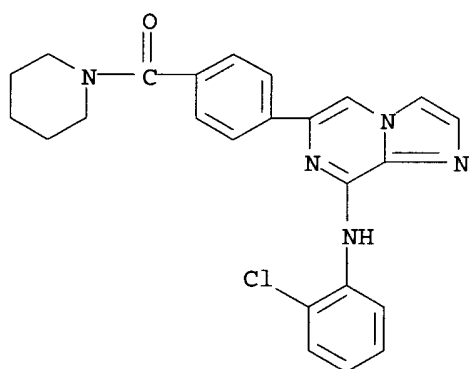
RN 618455-77-9 HCAPLUS

CN Piperidine, 1-[4-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



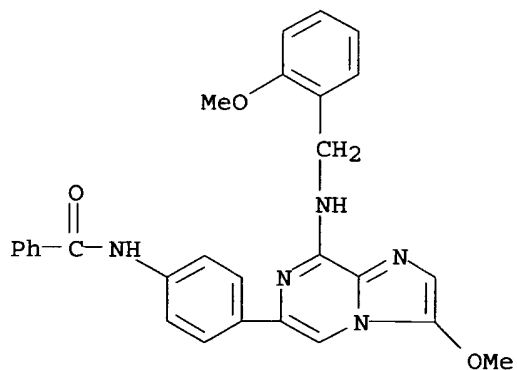
RN 618455-79-1 HCAPLUS

CN Piperidine, 1-[4-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]benzoyl]- (9CI) (CA INDEX NAME)



RN 618455-82-6 HCAPLUS

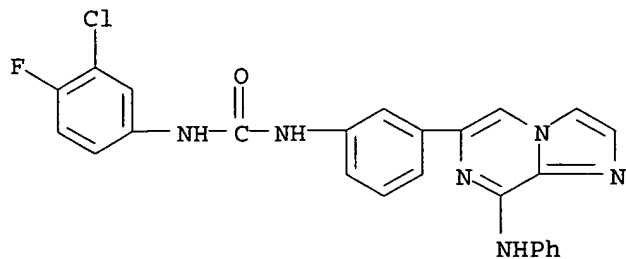
CN Benzamide, N-[4-[3-methoxy-8-[[(2-methoxyphenyl)methyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 618455-84-8 HCAPLUS

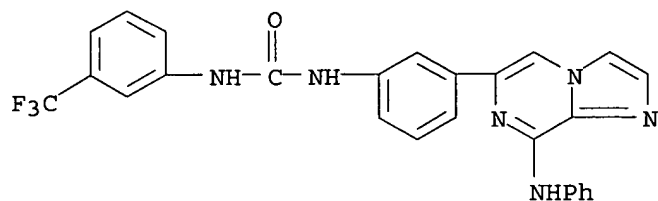
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a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



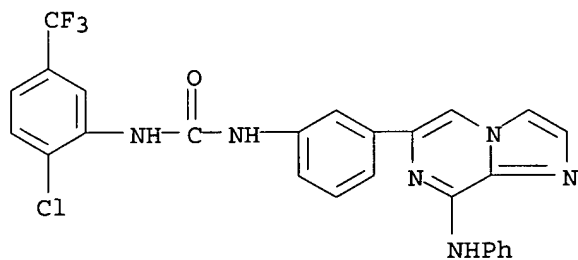
RN 618455-86-0 HCAPLUS

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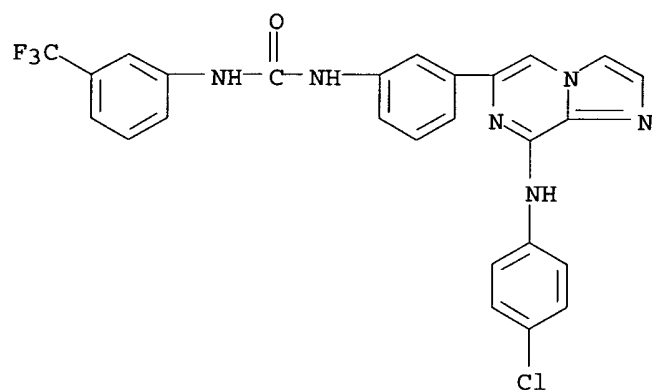
RN 618455-88-2 HCAPLUS

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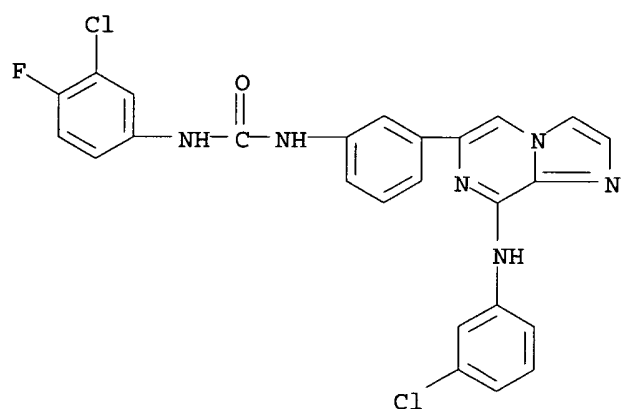
RN 618455-91-7 HCAPLUS

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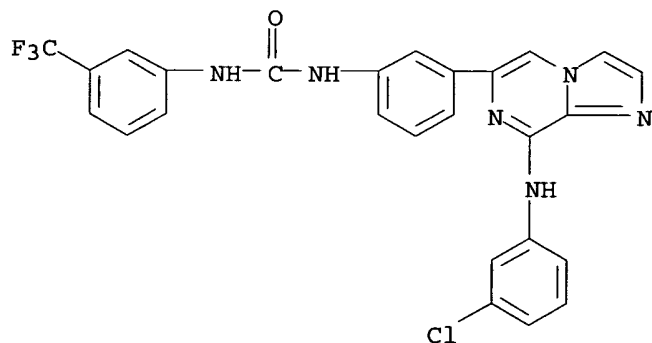
RN 618455-94-0 HCAPLUS

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RN 618455-97-3 HCAPLUS

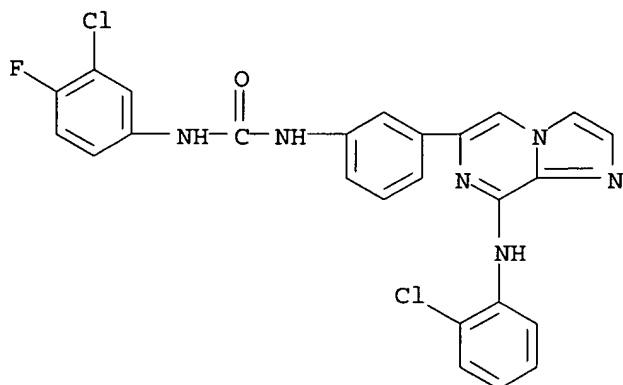
CN Urea, N-[3-[8-[(3-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]-N'-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 618455-99-5 HCAPLUS

CN Urea, N-(3-chloro-4-fluorophenyl)-N'-[3-[8-[(2-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

chlorophenyl) amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:594712 HCAPLUS

DOCUMENT NUMBER: 137:150267

TITLE: Methods using pyrazine compounds and pyridine compounds for inhibiting JAK kinases, compound preparation, and therapeutic use

INVENTOR(S): Burns, Christopher John; Wilks, Andrew Frederick

PATENT ASSIGNEE(S): Cytopia Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002060492 | A1 | 20020808 | WO 2002-AU89 | 20020130 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2436487 | AA | 20020808 | CA 2002-2436487 | 20020130 |
| EP 1363702 | A1 | 20031126 | EP 2002-715984 | 20020130 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2004528295 | T2 | 20040916 | JP 2002-560683 | 20020130 |
| US 2004102455 | A1 | 20040527 | US 2003-470955 | 20030730 |
| US 2006069084 | A1 | 20060330 | US 2005-223633 | 20050909 |
| PRIORITY APPLN. INFO.: | | | AU 2001-2792 | A 20010130 |
| | | | AU 2001-2793 | A 20010130 |
| | | | WO 2002-AU89 | W 20020130 |
| | | | US 2003-470955 | A3 20030730 |

OTHER SOURCE(S): MARPAT 137:150267

AB The invention provides methods of inhibiting JAK kinases involving the use of a group of compds. based either upon a 2-amino-6-carba-disubstituted pyrazine scaffold or a 2-amino-6-carba-disubstituted pyridine scaffold. The invention also provides methods of treating JAK-associated disease states.

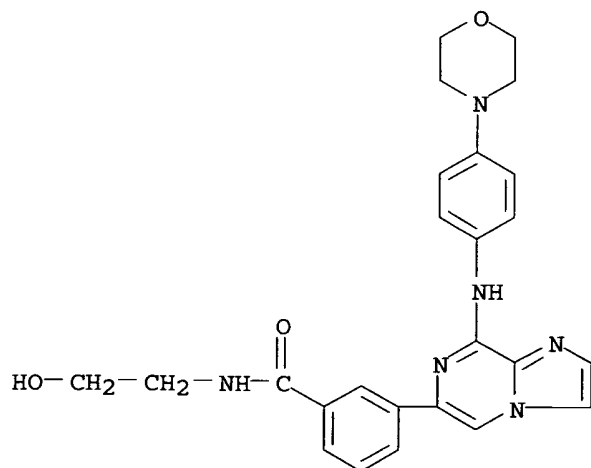
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

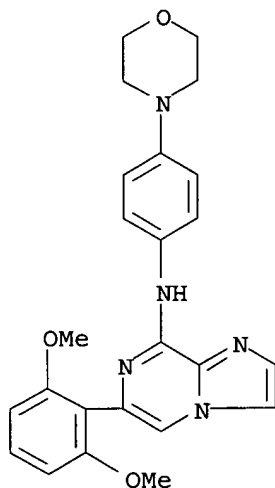
(pyrazine compds. and pyridine compds. for inhibiting JAK kinases, compound preparation, and therapeutic use)

RN 445263-58-1 HCAPLUS

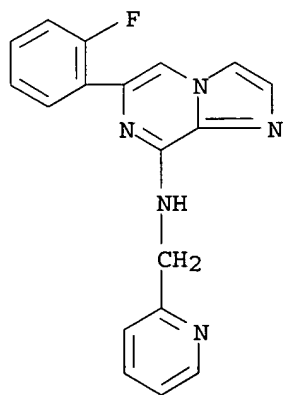
CN Benzamide, N-(2-hydroxyethyl)-3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



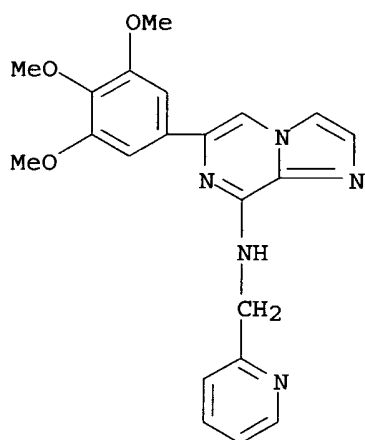
RN 445263-59-2 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2,6-dimethoxyphenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



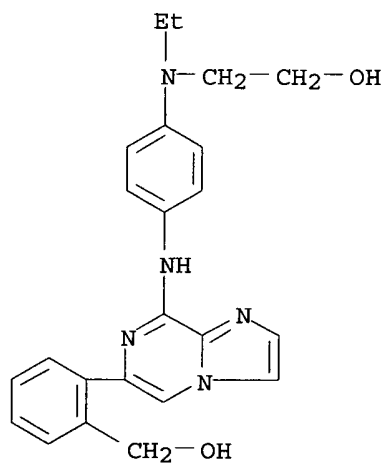
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 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



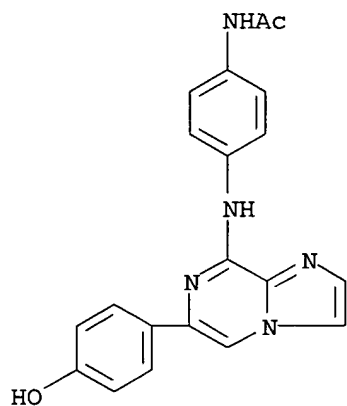
RN 445263-61-6 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-(2-pyridinylmethyl)-6-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 445263-62-7 HCAPLUS
 CN Benzenemethanol, 2-[8-[[4-[ethyl (2-hydroxyethyl) amino]phenyl] amino]imidazo
 [1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)

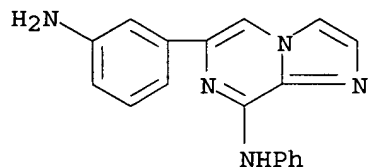


RN 445263-63-8 HCAPLUS
 CN Acetamide, N-[4-[[6-(4-hydroxyphenyl)imidazo[1,2-a]pyrazin-8-
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RN 445263-64-9 HCAPLUS

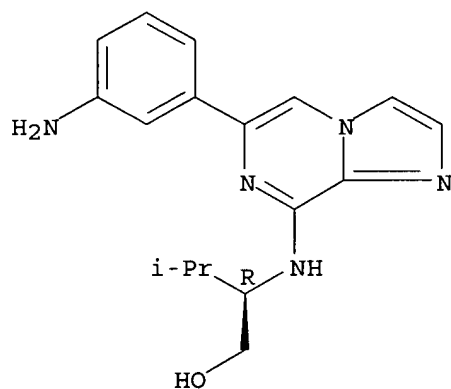
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-aminophenyl)-N-phenyl- (9CI) (CA INDEX NAME)



RN 445263-65-0 HCAPLUS

CN 1-Butanol, 2-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)

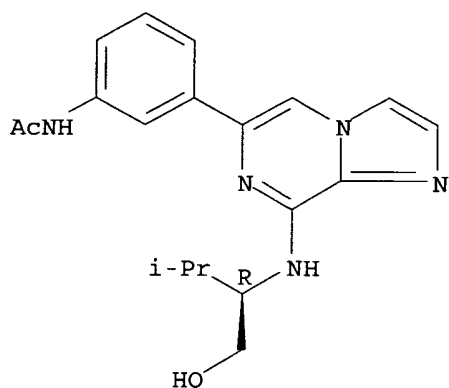
Absolute stereochemistry.



RN 445263-66-1 HCAPLUS

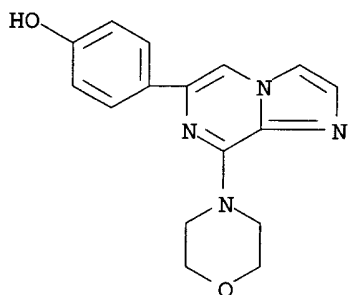
CN Acetamide, N-[3-[8-[[[(1R)-1-(hydroxymethyl)-2-methylpropyl]amino]imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 445263-67-2 HCAPLUS

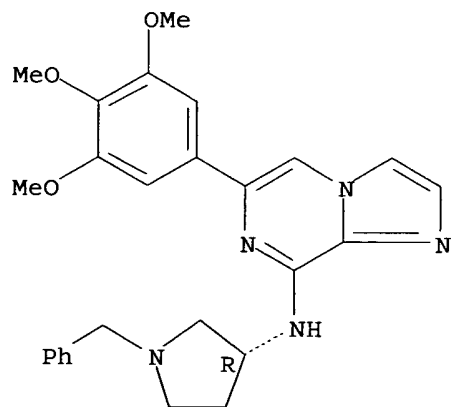
CN Phenol, 4-[8-(4-morpholinyl)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



RN 445263-69-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]-6-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

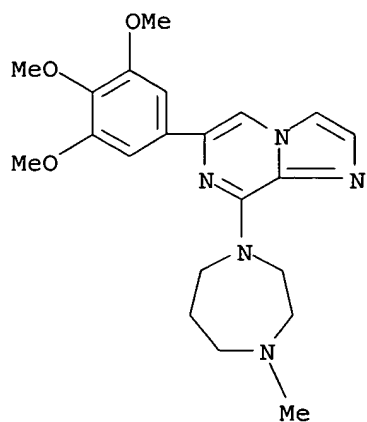
Absolute stereochemistry.



RN 445263-70-7 HCAPLUS

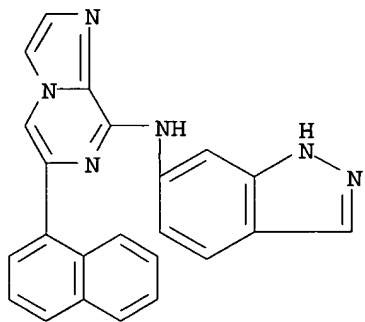
CN Imidazo[1,2-a]pyrazine, 8-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-

(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



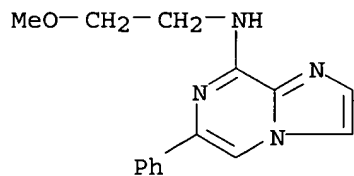
RN 445263-71-8 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-1H-indazol-6-yl-6-(1-naphthalenyl)- (9CI)
(CA INDEX NAME)



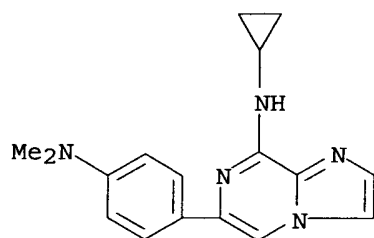
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CN Imidazo[1,2-a]pyrazin-8-amine, N-(2-methoxyethyl)-6-phenyl- (9CI) (CA INDEX NAME)



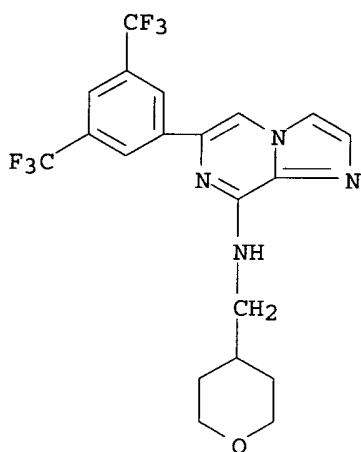
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CN Imidazo[1,2-a]pyrazin-8-amine, N-cyclopropyl-6-[4-(dimethylamino)phenyl]- (9CI) (CA INDEX NAME)



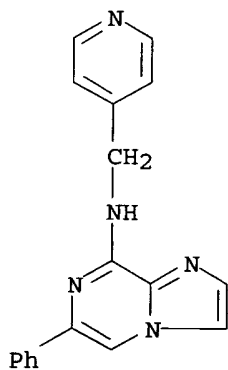
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3,5-bis(trifluoromethyl)phenyl]-N-[(tetrahydro-2H-pyran-4-yl)methyl]- (9CI) (CA INDEX NAME)



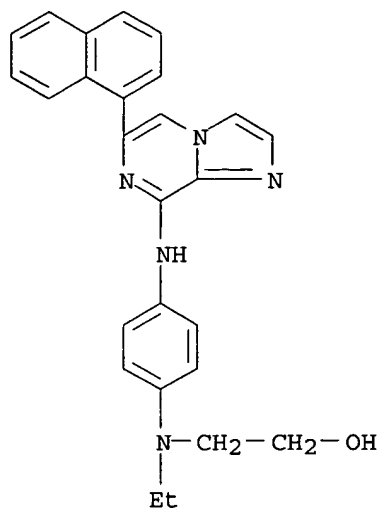
RN 445263-77-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-phenyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



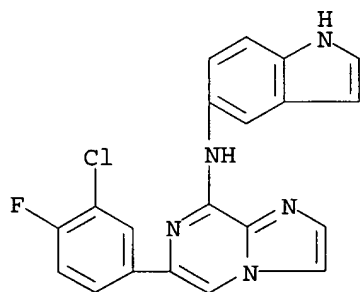
RN 445263-78-5 HCAPLUS

CN Ethanol, 2-[ethyl[4-[[6-(1-naphthalenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]amino]- (9CI) (CA INDEX NAME)



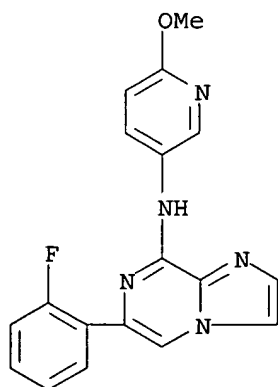
RN 445263-79-6 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-chloro-4-fluorophenyl)-N-1H-indol-5-yl-
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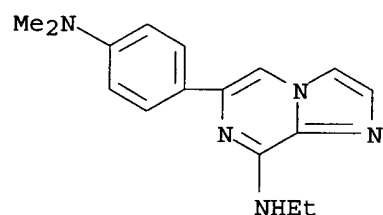
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-(6-methoxy-3-
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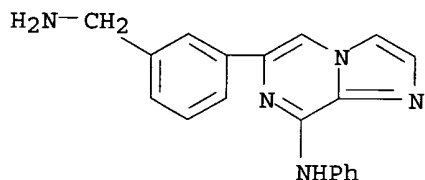
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-[4-(dimethylamino)phenyl]-N-ethyl- (9CI)
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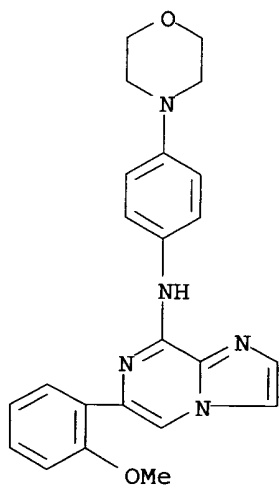
RN 445263-84-3 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3-(aminomethyl)phenyl]-N-phenyl- (9CI)
(CA INDEX NAME)



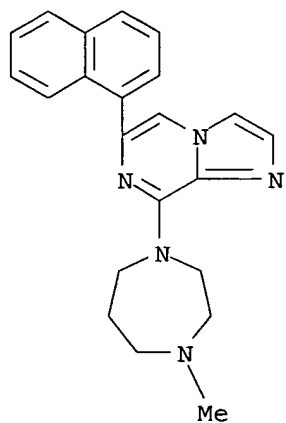
RN 445263-85-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-methoxyphenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)

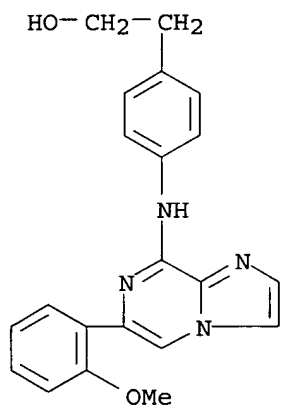


RN 445263-86-5 HCAPLUS

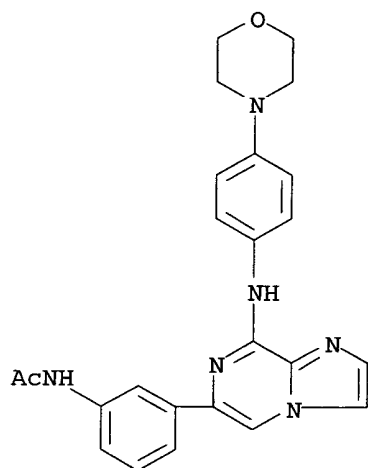
CN Imidazo[1,2-a]pyrazine, 8-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-(1-naphthalenyl)- (9CI) (CA INDEX NAME)



RN 445263-87-6 HCAPLUS
 CN Benzeneethanol, 4-[[6-(2-methoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino] -
 (9CI) (CA INDEX NAME)

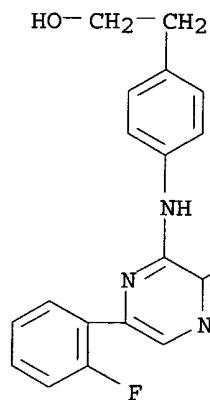


RN 445263-88-7 HCAPLUS
 CN Acetamide, N-[3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-
 yl]phenyl] - (9CI) (CA INDEX NAME)



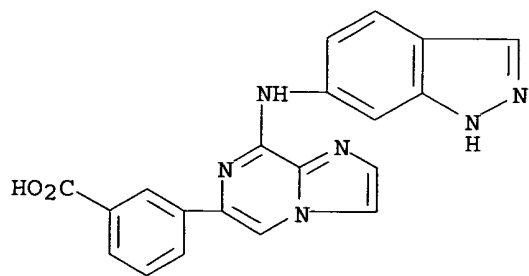
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CN Benzeneethanol, 4-[[6-(2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-(9CI) (CA INDEX NAME)



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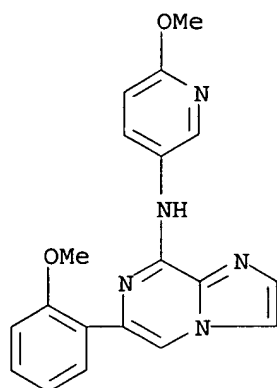
CN Benzoic acid, 3-[8-(1H-indazol-6-ylamino)imidazo[1,2-a]pyrazin-6-yl]-(9CI) (CA INDEX NAME)



RN 445263-91-2 HCAPLUS

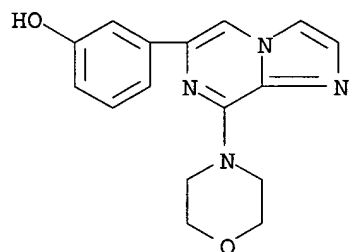
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-methoxyphenyl)-N-(6-methoxy-3-

pyridinyl)- (9CI) (CA INDEX NAME)



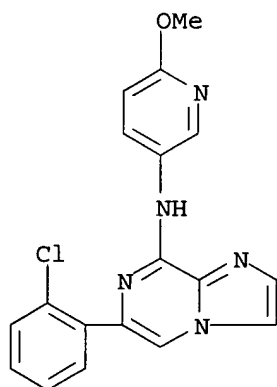
RN 445263-93-4 HCAPLUS

CN Phenol, 3-[8-(4-morpholinyl)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



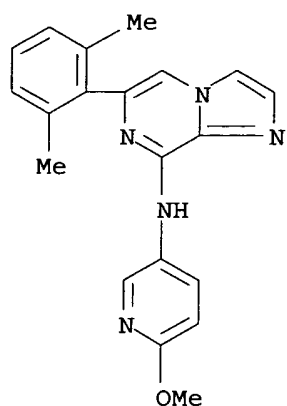
RN 445263-94-5 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



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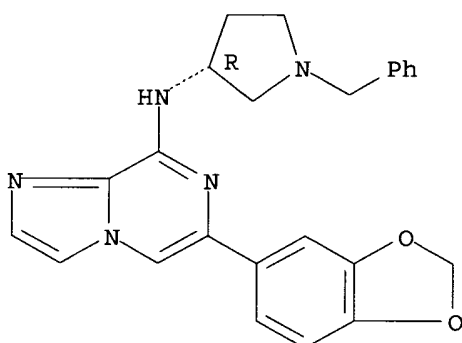
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2,6-dimethylphenyl)-N-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



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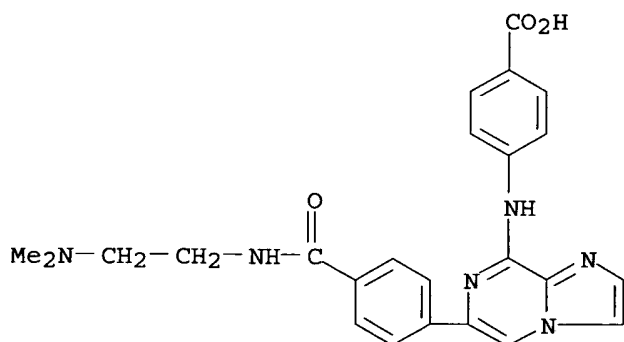
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



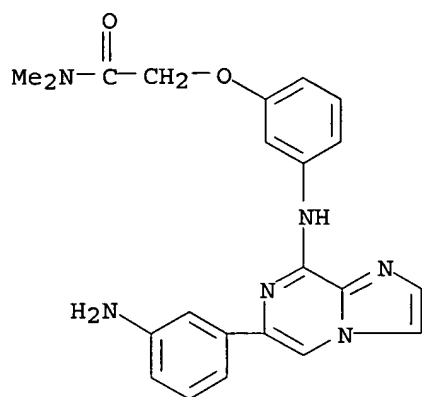
RN 445264-00-6 HCAPLUS

CN Benzoic acid, 4-[[[6-[4-[[[2-(dimethylamino)ethyl]amino]carbonyl]phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]benzoic acid] - (9CI) (CA INDEX NAME)



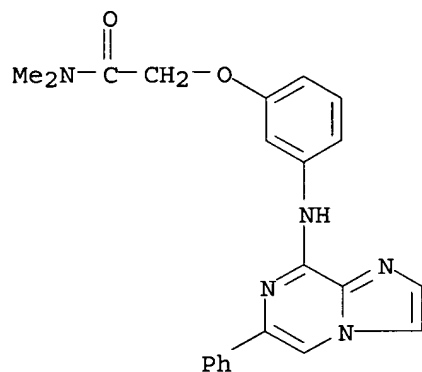
RN 445264-01-7 HCAPLUS

CN Acetamide, 2-[3-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



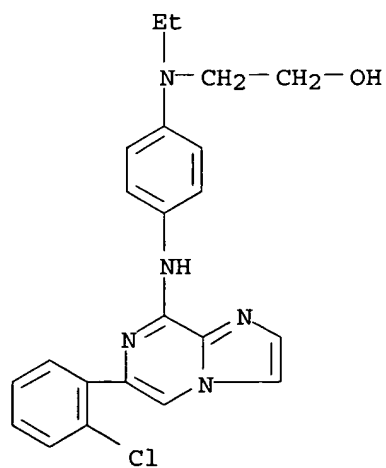
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CN Acetamide, N,N-dimethyl-2-[3-[(6-phenylimidazo[1,2-a]pyrazin-8-yl)amino]phenoxy]- (9CI) (CA INDEX NAME)



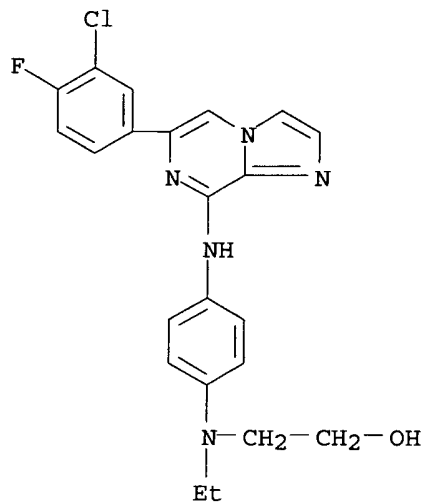
RN 445264-04-0 HCAPLUS

CN Ethanol, 2-[[4-[[6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



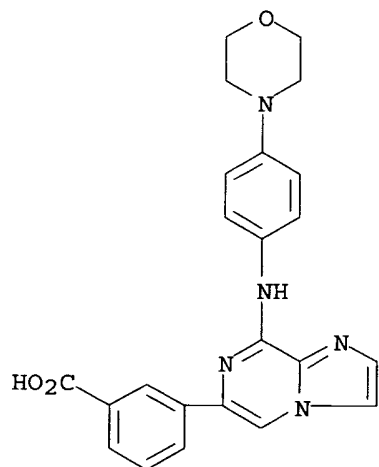
RN 445264-05-1 HCAPLUS

CN Ethanol, 2-[[4-[[6-(3-chloro-4-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



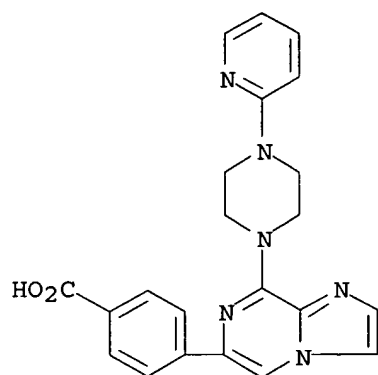
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CN Benzoic acid, 3-[8-[[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



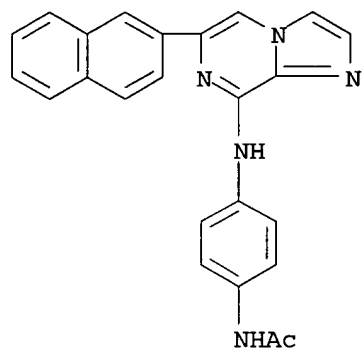
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CN Benzoic acid, 4-[8-[4-(2-pyridinyl)-1-piperazinyl]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



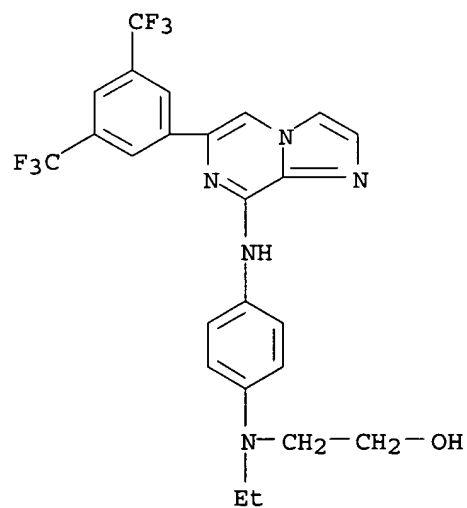
RN 445264-08-4 HCAPLUS

CN Acetamide, N-[4-[[6-(2-naphthalenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



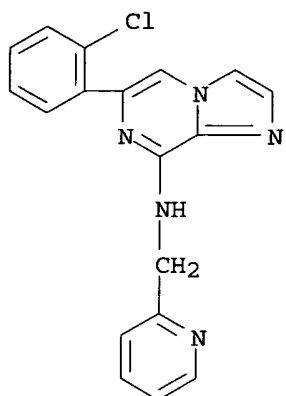
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CN Ethanol, 2-[[4-[[6-[3,5-bis(trifluoromethyl)phenyl]imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



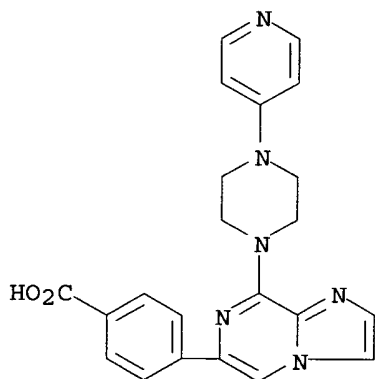
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-N-(2-pyridinylmethyl)-
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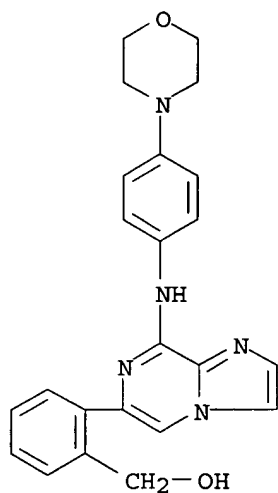
RN 445264-11-9 HCAPLUS

CN Benzoic acid, 4-[8-[4-(4-pyridinyl)-1-piperazinyl]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



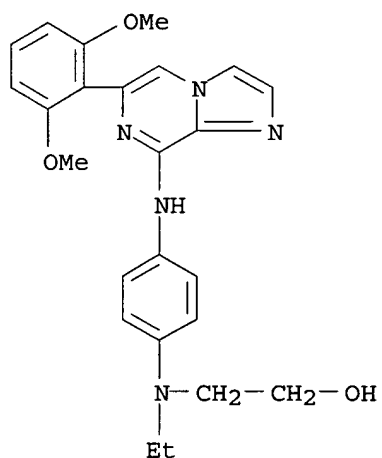
RN 445264-12-0 HCAPLUS

CN Benzenemethanol, 2-[8-[4-(4-morpholinyl)phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



RN 445264-13-1 HCAPLUS

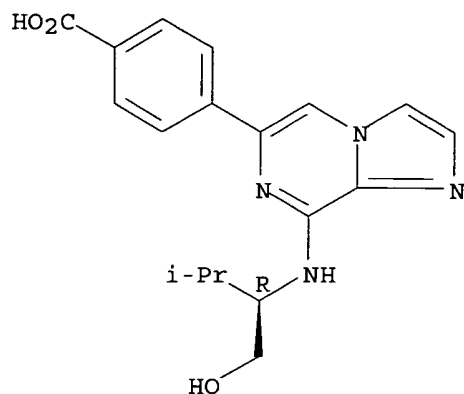
CN Ethanol, 2-[[4-[[6-(2,6-dimethoxyphenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]ethylamino]- (9CI) (CA INDEX NAME)



RN 445264-16-4 HCAPLUS

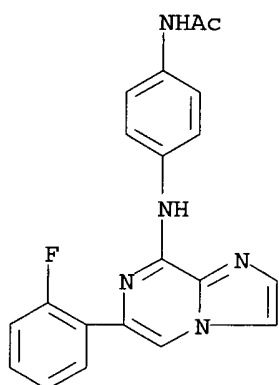
CN Benzoic acid, 4-[8-[[[(1R)-1-(hydroxymethyl)-2-methylpropyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



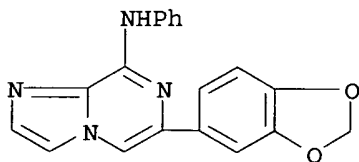
RN 445264-17-5 HCAPLUS

CN Acetamide, N-[4-[[6-(2-fluorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)



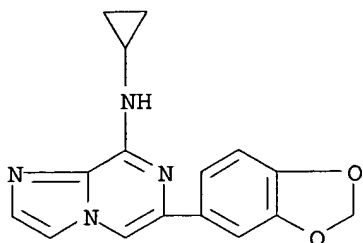
RN 445264-18-6 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-phenyl- (9CI) (CA INDEX NAME)

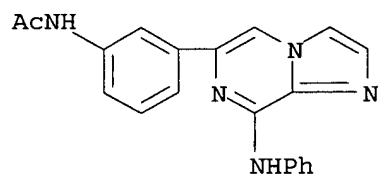


RN 445264-19-7 HCAPLUS

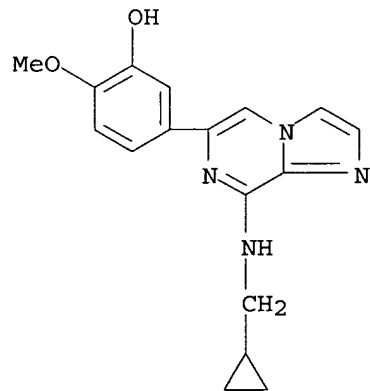
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-cyclopropyl- (9CI) (CA INDEX NAME)



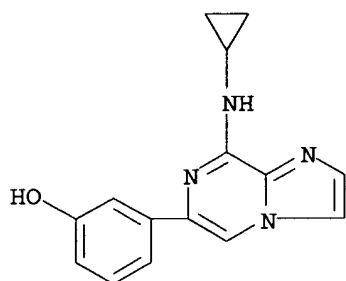
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 CN Acetamide, N-[3-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]phenyl]- (9CI)
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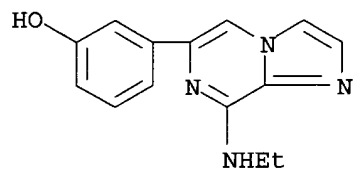
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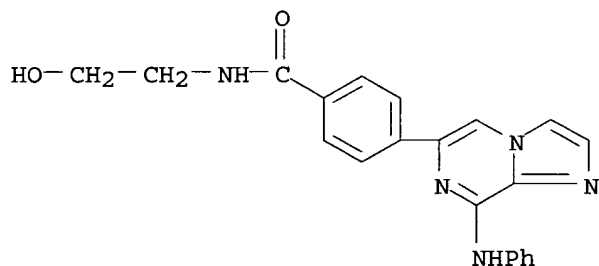
RN 445264-24-4 HCAPLUS
 CN Phenol, 3-[8-(cyclopropylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



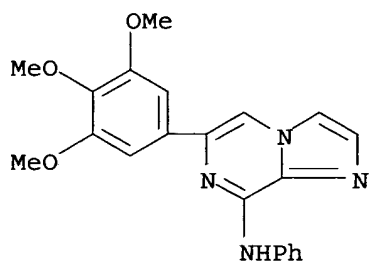
RN 445264-25-5 HCAPLUS
 CN Phenol, 3-[8-(ethylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



RN 445264-26-6 HCAPLUS
 CN Benzamide, N-(2-hydroxyethyl)-4-[8-(phenylamino)imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)

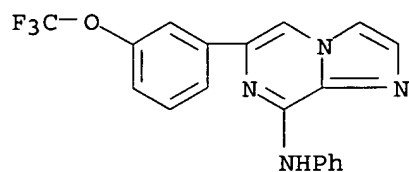


RN 445264-27-7 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-phenyl-6-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

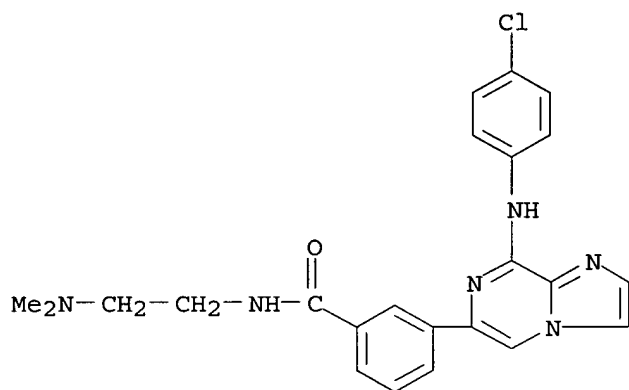


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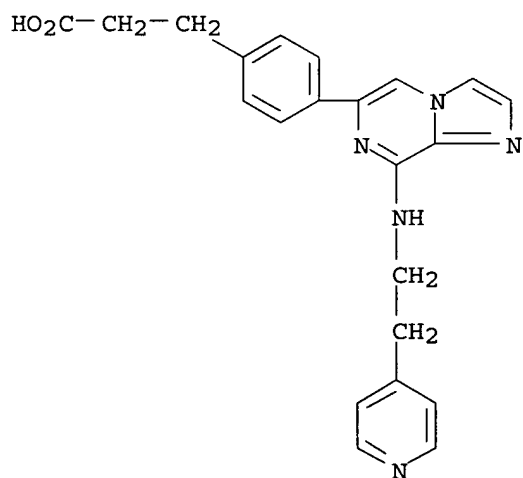
CN Imidazo[1,2-a]pyrazin-8-amine, N-phenyl-6-[3-(trifluoromethoxy)phenyl] -
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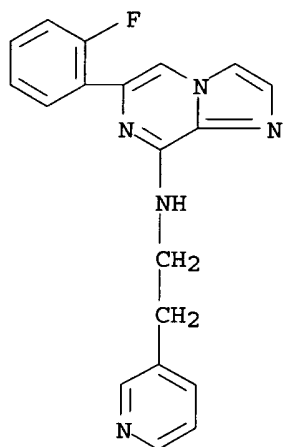
RN 445264-29-9 HCAPLUS
CN Benzamide, 3-[8-[(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-N-[2-(dimethylamino)ethyl] - (9CI) (CA INDEX NAME)



RN 445264-30-2 HCAPLUS
CN Benzenepropanoic acid, 4-[8-[[2-(4-pyridinyl)ethyl]amino]imidazo[1,2-a]pyrazin-6-yl] - (9CI) (CA INDEX NAME)

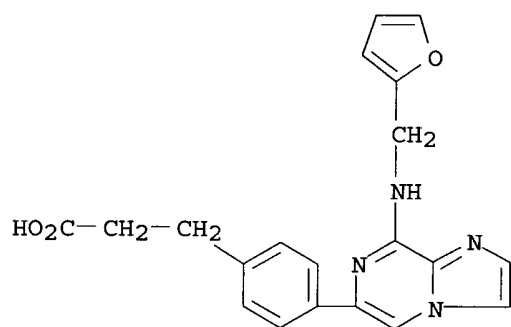


RN 445264-31-3 HCAPLUS
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(9CI) (CA INDEX NAME)



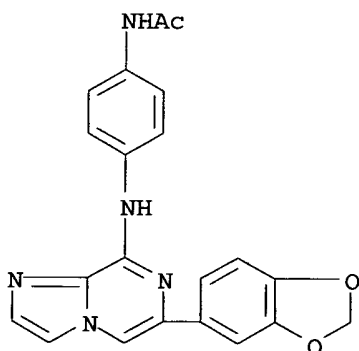
RN 445264-32-4 HCAPLUS

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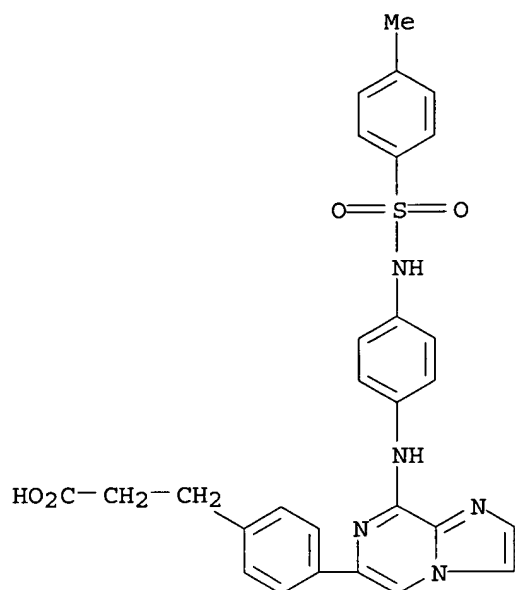
RN 445264-33-5 HCAPLUS

CN Acetamide, N-[4-[[6-(1,3-benzodioxol-5-yl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]- (9CI) (CA INDEX NAME)

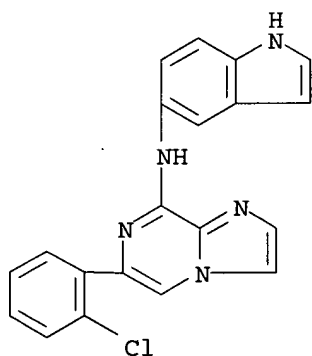


RN 445264-34-6 HCAPLUS

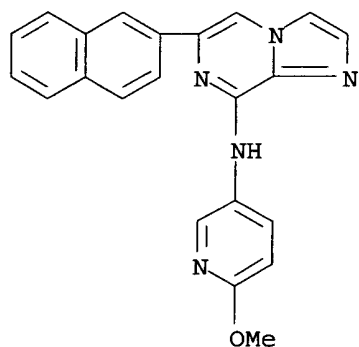
CN Benzenepropanoic acid, 4-[8-[[4-[[[4-methylphenyl)sulfonyl]amino]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



RN 445264-35-7 HCAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-chlorophenyl)-N-1H-indol-5-yl- (9CI)
(CA INDEX NAME)

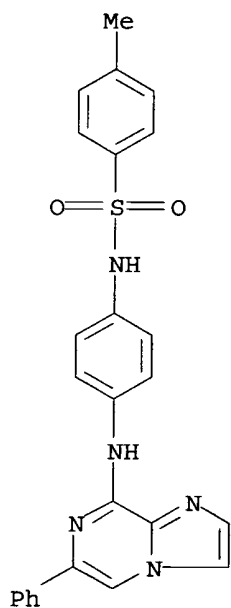


RN 445264-36-8 HCAPLUS
CN Imidazo[1,2-a]pyrazin-8-amine, N-(6-methoxy-3-pyridinyl)-6-(2-naphthalenyl)- (9CI) (CA INDEX NAME)



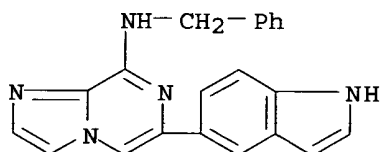
RN 445264-37-9 HCAPLUS

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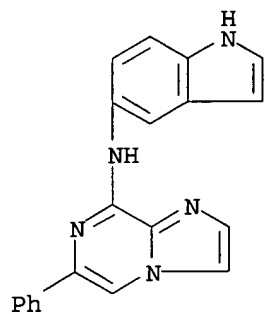
RN 445264-38-0 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1H-indol-5-yl)-N-(phenylmethoxy)- (9CI) (CA INDEX NAME)



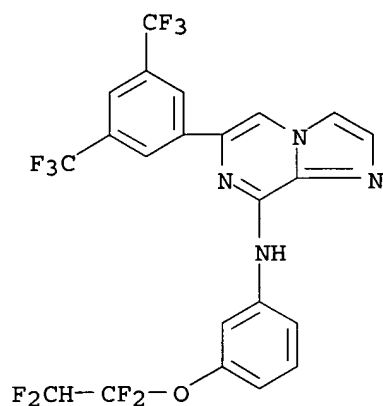
RN 445264-39-1 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, N-1H-indol-5-yl-6-phenyl- (9CI) (CA INDEX NAME)



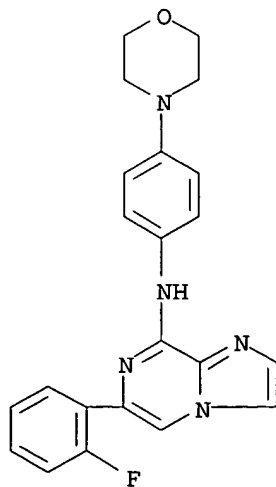
RN 445264-40-4 HCAPLUS

CN Imidazo[1,2-a]pyrazin-8-amine, 6-[3,5-bis(trifluoromethyl)phenyl]-N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]- (9CI) (CA INDEX NAME)



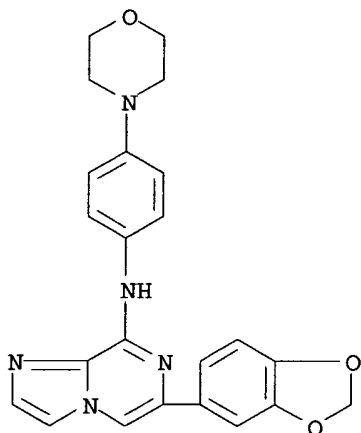
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(2-fluorophenyl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



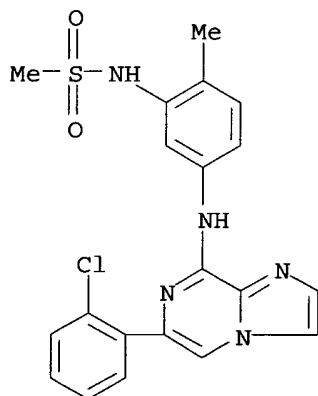
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CN Imidazo[1,2-a]pyrazin-8-amine, 6-(1,3-benzodioxol-5-yl)-N-[4-(4-morpholinyl)phenyl]- (9CI) (CA INDEX NAME)



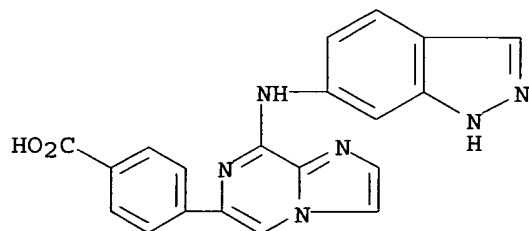
RN 445264-43-7 HCAPLUS

CN Methanesulfonamide, N-[5-[[6-(2-chlorophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]-2-methylphenyl]- (9CI) (CA INDEX NAME)



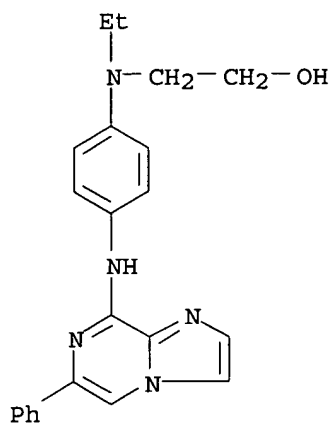
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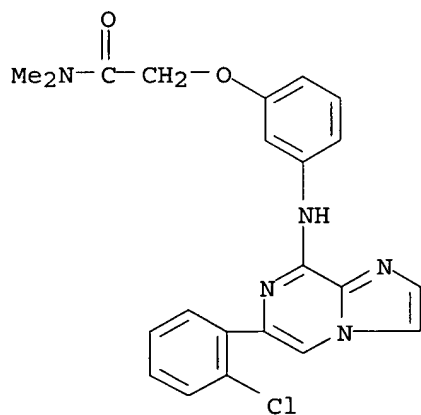
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CN Ethanol, 2-[ethyl[4-[(6-phenylimidazo[1,2-a]pyrazin-8-yl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)



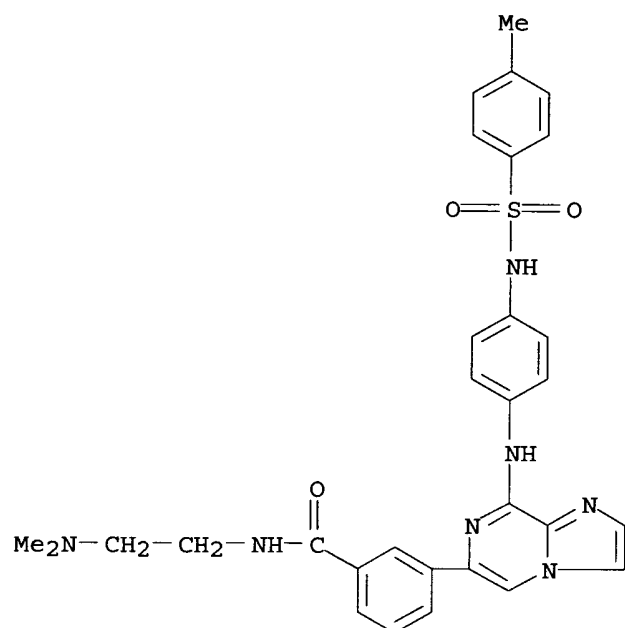
RN 445264-47-1 HCAPLUS

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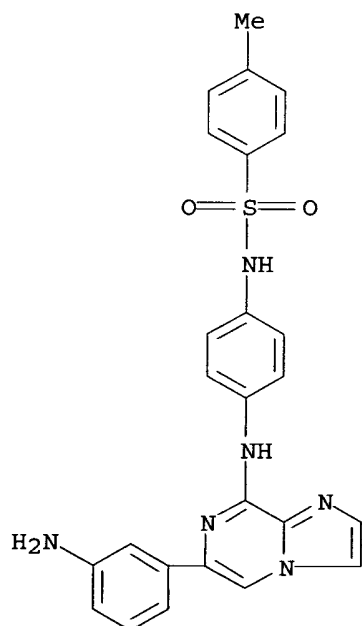
RN 445264-48-2 HCAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-3-[8-[[4-[[4-(4-methylphenyl)sulfonyl]amino]phenyl]amino]imidazo[1,2-a]pyrazin-6-yl]- (9CI) (CA INDEX NAME)



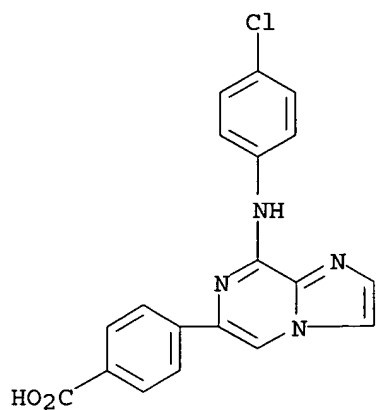
RN 445264-50-6 HCAPLUS

CN Benzenesulfonamide, N-[4-[[6-(3-aminophenyl)imidazo[1,2-a]pyrazin-8-yl]amino]phenyl]-4-methyl- (9CI) (CA INDEX NAME)

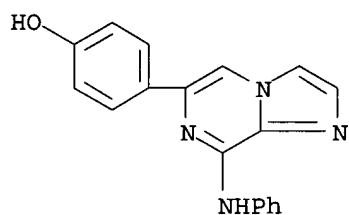


RN 445264-51-7 HCAPLUS

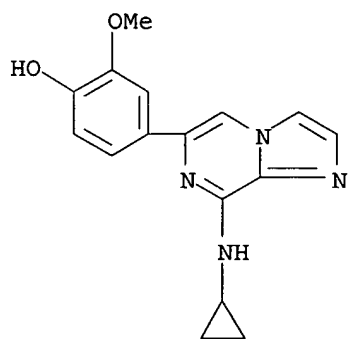
CN Benzoic acid, 4-[8-[[4-(4-chlorophenyl)amino]imidazo[1,2-a]pyrazin-6-yl]-4-aminophenyl]- (9CI) (CA INDEX NAME)



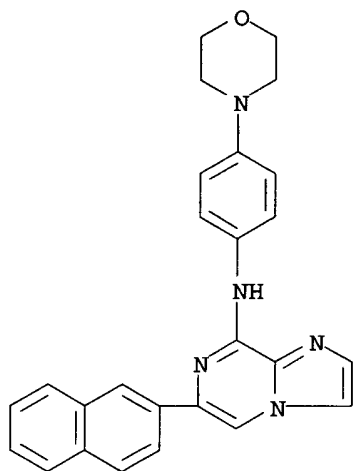
RN 445264-52-8 HCAPLUS
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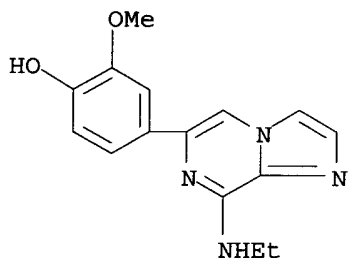
RN 445264-54-0 HCAPLUS
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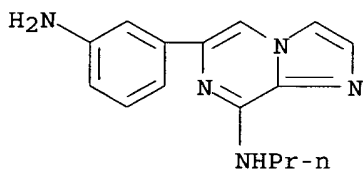
RN 445264-55-1 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, N-[4-(4-morpholinyl)phenyl]-6-(2-naphthalenyl)- (9CI) (CA INDEX NAME)



RN 445264-56-2 HCAPLUS
 CN Phenol, 4-[8-(ethylamino)imidazo[1,2-a]pyrazin-6-yl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 445264-57-3 HCAPLUS
 CN Imidazo[1,2-a]pyrazin-8-amine, 6-(3-aminophenyl)-N-propyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

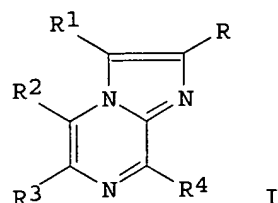
ACCESSION NUMBER: 1983:83223 HCAPLUS

DOCUMENT NUMBER: 98:83223

TITLE: Piperazinyimidazo[1,2-a]pyrazines with selective affinity for in vitro α -adrenergic receptor subtypes

AUTHOR(S): Lumma, William C., Jr.; Randall, William C.; Cresson, E. L.; Huff, Joel R.; Hartman, Richard D.; Lyon, T. F.

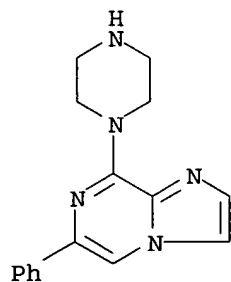
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA,
19486, USA
SOURCE: Journal of Medicinal Chemistry (1983), 26(3), 357-63
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 98:83223
GI



AB The title compds. I (R = H, etc.; R1 = H, Cl, Me, etc.; R2 = H, piperazinyl, etc.; R3 = H, Cl, Ph, piperazinyl; R4 = H, piperazino or methylpiperazino) were prepared and evaluated in vitro for their affinity for α_1 - and α_2 -adrenergic receptors. 8-(1-piperazinyl)imidazo[1,2-a]pyrazine (II) [76537-53-6] was .apprx.70 times more selective than mianserin for the α_2 -receptor. Computer-assisted mol. modeling techniques were used to describe possible preferred conformations for receptor binding. Regioselective syntheses of the heterocyclic ring system are given. Literature NMR assignments for the imidazo[1,2-a]pyrazine ring system were made. Conformational energies for II and its 5-position isomer in relation to the semirigid mianserin were estimated. Structure-activity relations are discussed.

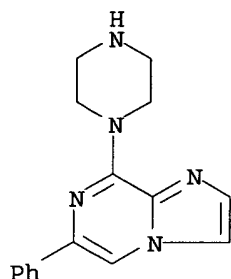
IT **84066-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and sympathomimetic activity of)

RN 84066-01-3 HCAPLUS
CN Imidazo[1,2-a]pyrazine, 6-phenyl-8-(1-piperazinyl)- (9CI) (CA INDEX NAME)



IT **84066-00-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 84066-00-2 HCAPLUS
CN Imidazo[1,2-a]pyrazine, 6-phenyl-8-(1-piperazinyl)-, monohydrochloride
(9CI) (CA INDEX NAME)



● HCl

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L1      STR
L3      570 SEA FILE=REGISTRY SSS FUL L1
L4      15 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
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        ROBERT"/AU OR ("DESIMONE ROBERT W"/AU OR "DESIMONE ROBERT
        WALTER JR"/AU)
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        ANTHONY IRWIN"/AU)
L7      26 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DARROW J W"/AU OR "DARROW
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L8      172 SEA FILE=HCAPLUS ABB=ON PLU=ON "MITCHELL S"/AU OR "MITCHELL
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L9      24 SEA FILE=HCAPLUS ABB=ON PLU=ON "CURRIE K P M"/AU OR "CURRIE
        K S"/AU OR "CURRIE KEVIN"/AU OR "CURRIE KEVIN S"/AU
L10     1 SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 AND L6 AND L7 AND L8 AND
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L11     5 SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 AND (L6 OR L7 OR L8 OR
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L12     3 SEA FILE=HCAPLUS ABB=ON PLU=ON (L6 AND (L7 OR L8 OR L9)) NOT
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L13     3 SEA FILE=HCAPLUS ABB=ON PLU=ON (L7 AND (L8 OR L9)) NOT L4
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L15     8 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 OR L11 OR L12 OR L13 OR
        L14

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L15 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1319153 HCAPLUS
 DOCUMENT NUMBER: 144:191989
 TITLE: Synthetic studies in phytochrome chemistry
 AUTHOR(S): Jacobi, Peter A.; Adel Odeh, Imad M.; Buddhu, Subhas
 C.; Cai, Guolin; Rajeswari, Sundaramoorthi; Fry,
 Douglas; Zheng, Wanjun; DeSimone, Robert W.;
 Guo, Jiasheng; Coutts, Lisa D.; Hauck, Sheila I.;
 Leung, Sam H.; Ghosh, Indranath; Pippin,
 Douglas

CORPORATE SOURCE: Department of Chemistry, Dartmouth College, Hanover,
NH, 03755, USA
SOURCE: Synlett (2005), (19), 2861-2885
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

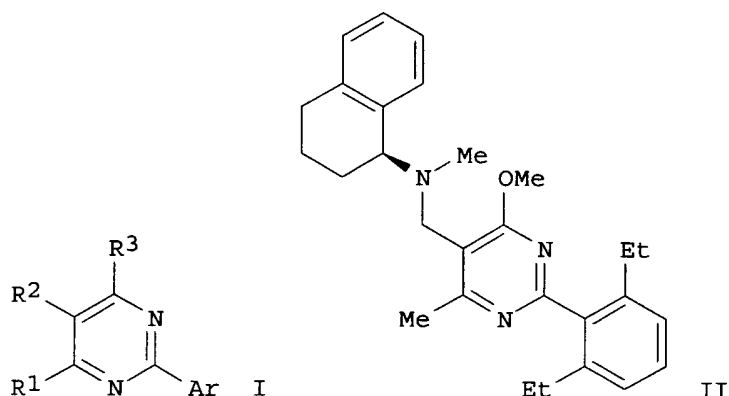
AB A review. An account is given of the author's several approaches to the synthesis of the parent chromophore of phytochrome (1), a protein-bound linear tetrapyrrole derivative that controls photomorphogenesis in higher plants. These studies culminated in enantioselective syntheses of both (2R)- and (2S)-phytochromobilin (4), as well as several ¹³C-labeled derivs. designed to probe the site of Z,E-isomerization during photoexcitation. When reacted in vitro, synthetic 2R-4 and recombinant-derived phytochrome apoprotein N-C produced a protein-bound chromophore with identical difference spectra to naturally occurring 1.

REFERENCE COUNT: 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L15 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1241187 HCAPLUS
DOCUMENT NUMBER: 144:6804
TITLE: Preparation of 4,5-disubstituted-2-aryl pyrimidines as C5a receptor ligands
INVENTOR(S): Maynard, George D.; Ghosh, Manuka; Yuan, Jun;
Currie, Kevin S.; Mitchell, Scott;
Guo, Qin; Zhao, He
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2005110416 | A2 | 20051124 | WO 2005-US15897 | 20050506 |
| WO 2005110416 | A3 | 20060413 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005277654 | A1 | 20051215 | US 2005-123755 | 20050506 |
| PRIORITY APPLN. INFO.: | | | US 2004-569222P | P 20040508 |
| | | | US 2005-649973P | P 20050204 |
| OTHER SOURCE(S): MARPAT 144:6804 | | | | |
| GI | | | | |



AB Title compds. I [Ar = mono-, di-, or tri-substituted Ph, (un)substituted naphthyl or heteroaryl; R¹ = H, (un)substituted alkyl, alkenyl, alkynyl, etc.; R² = OH, CHO, (un)substituted alkyl, etc.; R³ = (un)substituted aryl, cycloalkyl, arylalkyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as C5a receptor ligands. Thus, e.g., II was prepared by substitution of 2,4-dichloro-5-chloromethyl-6-methylpyrimidine (preparation given) with (1S)-methyl-(1,2,3,4-tetrahydronaphthalen-1-yl)amine followed by substitution of the 4-chloro group with methanol and coupling with 2,6-diethylphenylboronic acid. Preferred compds. of the invention bind to C5a receptors with high affinity and exhibit neutral antagonist or inverse activity at C5a receptors. I exhibited IC₅₀ values of 2 μ M or less in calcium immobilization assays. The present invention also relates to pharmaceutical compns. comprising such compds., and to the use of such compds. in treating a variety of inflammatory, cardiovascular, and immune system disorders. In addition, the present invention provides labeled 4,5-disubstituted-2-arylpyrimidines, which are useful as probes for the localization of C5a receptors.

L15 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:713308 HCAPLUS

DOCUMENT NUMBER: 141:235471

TITLE: Privileged structures: Applications in drug discovery

AUTHOR(S): DeSimone, R. W.; Currie, K. S.;

Mitchell, S. A.; Darrow, J. W.;

Pippin, D. A.

CORPORATE SOURCE: Cellular Genomics Inc., Branford, CT, 06405, USA

SOURCE: Combinatorial Chemistry and High Throughput Screening (2004), 7(5), 473-493

CODEN: CCHSFU; ISSN: 1386-2073

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Over the past 15 yr the privileged structure concept has emerged as a fruitful approach to the discovery of novel biol. active mols. Privileged structures are mol. scaffolds with versatile binding properties, such that a single scaffold is able to provide potent and selective ligands for a range of different biol. targets through modification of functional groups. In addition, privileged structures typically exhibit good drug-like properties, which in turn leads to more drug-like compound libraries and leads. The net result is the production of high quality leads that provide a solid foundation for further

development. The identification of privileged structures will be discussed, emphasizing the importance of understanding the structure-target relationships that confer "privileged" status. This understanding allows privileged structure based libraries to be targeted at distinct target families (e.g. GPCRs, LGIC, enzymes/kinases). Privileged structures have been successfully exploited across and within different target families and promises to be an effective approach to the discovery and optimization of novel bioactive mols. The application of the privileged structure approach, both in traditional medicinal chemical and in the design of focused libraries, will be discussed with the aid of illustrative examples.

REFERENCE COUNT: 146 THERE ARE 146 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2866 HCAPLUS

DOCUMENT NUMBER: 140:77168

TITLE: Certain aromatic monocycles, particularly trisubstituted [1,3,5]triazine derivatives, as kinase modulators, and their pharmaceutical compositions and methods of use

INVENTOR(S): Darrow, James W.; Desimone, Robert W.; Pippin, Douglas A.; Mitchell, Scott A.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2004000820 | A2 | 20031231 | WO 2003-US19961 | 20030623 |
| WO 2004000820 | A3 | 20040325 | | |
| W: | | | | |
| AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: | | | | |
| GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003245669 | A1 | 20040106 | AU 2003-245669 | 20030623 |
| US 2004082627 | A1 | 20040429 | US 2003-602559 | 20030623 |
| PRIORITY APPLN. INFO.: | | | US 2002-390626P | P 20020621 |
| | | | WO 2003-US19961 | W 20030623 |

OTHER SOURCE(S): MARPAT 140:77168

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I are useful as modulators of kinase activity [wherein: one

of R1, R2, and R3 may = H, alkyl, (hetero)cycloalkyl, cycloalkylmethyl, alkoxy, alkoxyalkoxy, sulfonamide; otherwise, R1, R2, R3 = (un)substituted (di)alkylamino, Ph, PhCH2, heteroaryl, heteroaryloxy, PhOC6H4, 4-phenylpiperazin-1-yl, 4-heteroarylpiperazin-1-yl; n = 0 or 1; Z1, Z2, Z3 = NR4, O, X(:O), SO2, NR5X(:O), X(:O)NR6, NR7SO2, SO2NR8, NR9CONR10; X = C or S; R4-R10 = H, alkyl, (un)substituted Ph, PhCH2, heteroaryl; m = 0 or 1; W = 1,3,5-benzenetriyl, 1,3,5-triazine-2,4,6-triyl, 2,4,6-pyrimidinetriyl, 2,4,6-pyridinetriyl, 6-oxo-1,6-dihydropyridazine-3,5-diyl, pyrazine-2,6-diyl, pyridine-3,5-diyl, pyridazine-3,5-diyl; including pharmaceutically acceptable salts, hydrates, solvates, crystal forms, diastereomers, prodrugs, and mixts.]. Several brief synthetic examples and a listing of approx. 20 compds. are given. For instance, reaction of 2,4,6-trichloro-[1,3,5]triazine with 2-methoxybenzylamine and NaHCO3 in MeCN at 0° gave intermediate II, which was coupled with excess 4-PhOC6H4B(OH)2 in the presence of Pd(PPh3)4 and Na2CO3 to give invention compound III. In bioassays against human recombinant AKT-1 kinase, all exemplified compds. I had IC50 values of ≤ 25 μM.

L15 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2701 HCAPLUS
 DOCUMENT NUMBER: 140:53404
 TITLE: Amino-substituted monocycles as AKT-1 kinase modulators
 INVENTOR(S): Darrow, James W.; Desimone, Robert W.; Pippin, Douglas A.; Mitchell, Scott A.
 PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA
 SOURCE: PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2004000318 | A2 | 20031231 | WO 2003-US19978 | 20030623 |
| WO 2004000318 | A3 | 20040408 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2003249369 | A1 | 20040106 | AU 2003-249369 | 20030623 |
| US 2004053927 | A1 | 20040318 | US 2003-602560 | 20030623 |
| US 7015227 | B2 | 20060321 | | |

PRIORITY APPLN. INFO.: US 2002-390628P P 20020621
 WO 2003-US19978 W 20030623

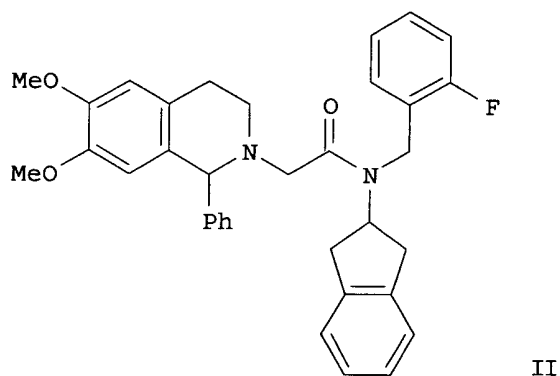
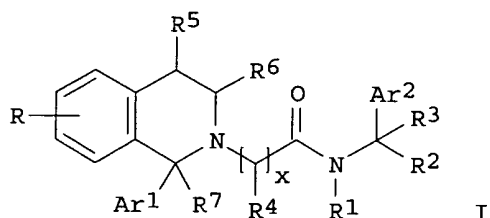
OTHER SOURCE(S): MARPAT 140:53404

AB A composition comprises amino-substituted monocycle, a pharmaceutically acceptable salt, hydrate, solvate, crystal form, diastereomer, prodrug, or mixture thereof. The compds. are of utility as modulators of kinase activity.

L15 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:796667 HCAPLUS
 DOCUMENT NUMBER: 139:307693
 TITLE: Preparation of substituted tetrahydroisoquinolines as
 C5a receptor modulators
 INVENTOR(S): Mitchell, Scott; Ohliger, Robert; Zhang,
 Luyan; Zhao, He; Currie, Kevin; Lee, Kyungae
 PATENT ASSIGNEE(S): Neurogen Corporation, USA
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|-------------|
| WO 2003082828 | A1 | 20031009 | WO 2003-US9046 | 20030325 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2479930 | AA | 20031009 | CA 2003-2479930 | 20030325 |
| AU 2003218374 | A1 | 20031013 | AU 2003-218374 | 20030325 |
| EP 1487798 | A1 | 20041222 | EP 2003-714371 | 20030325 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006508894 | T2 | 20060316 | JP 2003-580296 | 20030325 |
| US 2004006069 | A1 | 20040108 | US 2003-401135 | 20030327 |
| US 6777422 | B2 | 20040817 | | |
| US 2004204446 | A1 | 20041014 | US 2004-824826 | 20040415 |
| US 6916830 | B2 | 20050712 | | |
| PRIORITY APPLN. INFO.: | | | US 2002-368199P | P 20020328 |
| | | | WO 2003-US9046 | W 20030325 |
| | | | US 2003-401135 | A1 20030327 |
| OTHER SOURCE(S): | | | MARPAT 139:307693 | |
| GI | | | | |



AB The title compds. [I; x = 1-3; R = halo, OH, alkoxy, etc.; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, halo, alkyl, alkoxy; R5, R6 = H, halo, OH, etc.; R7 = H, alkyl, alkenyl, etc.; Ar1 = (un)substituted Ph, naphthyl, biphenyl, etc.; Ar2 = (un)unsubstituted aryl, heteroaryl] which are ligands that may be used to modulate C5a receptor activity in vivo or in vitro, and are particularly useful in the treatment of conditions associated with pathol. C5a receptor activation in humans, domesticated companion animals and livestock animals, were prepared Thus, reacting 6,7-dimethoxy-1-phenyl-1,2,3,4-tetrahydroisoquinoline.HCl with N-(1-fluorobenzyl)-N-(indan-2-yl)-2-bromoacetamide in the presence of K2CO3 in MeCN afforded II. Preferred compds. I exhibit IC50 values of less than 1 μ M in the assay for C5a receptor mediated chemotaxis. Pharmaceutical compns. and methods for using them to treat disorders associated with pathol. C5a receptor activation are provided, as are methods for using such ligands for receptor localization studies.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:487553 HCAPLUS

DOCUMENT NUMBER: 137:47200

TITLE: Aryl or heteroaryl fused imidazoles as selective GABAA receptor ligands

INVENTOR(S): Li, Guiying; Peterson, John M.; Albaugh, Pamela; Currie, Kevin S.; Cai, Guolin; Gustavson, Linda M.; Lee, Kyungae; Hutchison, Alan; Singh, Vinod; Maynard, George D.; Yuan, Jun; Ling, Hong Xie; Ghosh, Manuka; Liu, Nian; Luke, George P.; Mitchell, Scott; Allen, Martin Patrick; Liras, Spiros

PATENT ASSIGNEE(S): Neurogen Corporation, USA; Pfizer Inc.

SOURCE: PCT Int. Appl., 309 pp.

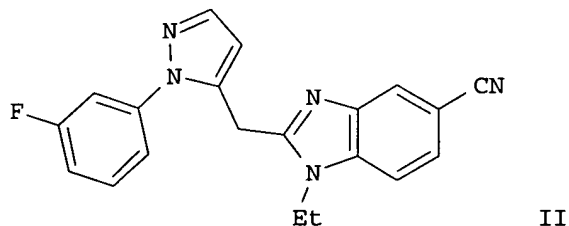
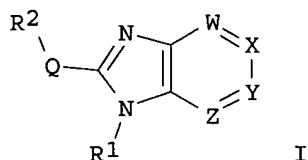
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

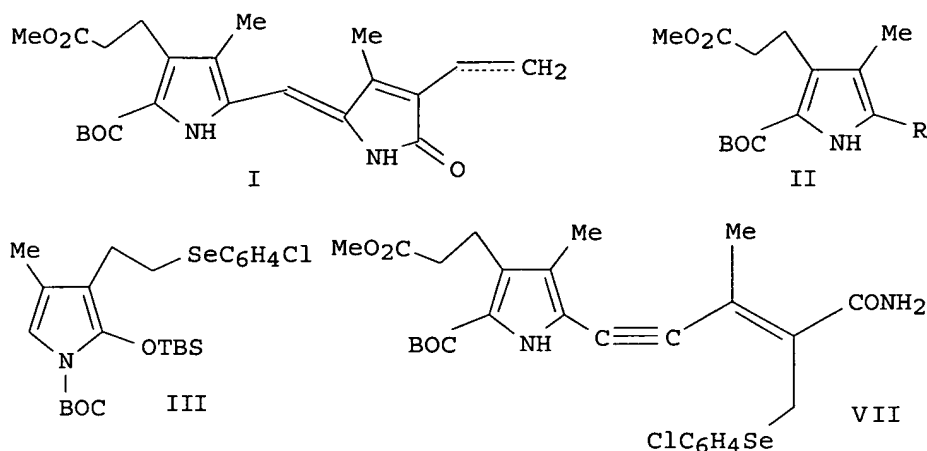
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 2002050062 | A2 | 20020627 | WO 2001-US50038 | 20011221 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2431592 | AA | 20020627 | CA 2001-2431592 | 20011221 |
| AU 2002032768 | A5 | 20020701 | AU 2002-32768 | 20011221 |
| US 2003069257 | A1 | 20030410 | US 2001-38069 | 20011221 |
| US 6916819 | B2 | 20050712 | | |
| EP 1368342 | A2 | 20031210 | EP 2001-992307 | 20011221 |
| EP 1368342 | B1 | 20050907 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| EE 200300304 | A | 20031215 | EE 2003-304 | 20011221 |
| CN 1553909 | A | 20041208 | CN 2001-822386 | 20011221 |
| JP 2004536782 | T2 | 20041209 | JP 2002-551558 | 20011221 |
| AT 304008 | E | 20050915 | AT 2001-992307 | 20011221 |
| BR 2001016385 | A | 20051213 | BR 2001-16385 | 20011221 |
| BG 107899 | A | 20040831 | BG 2003-107899 | 20030611 |
| ZA 2003004544 | A | 20050407 | ZA 2003-4544 | 20030611 |
| NO 2003002834 | A | 20030808 | NO 2003-2834 | 20030620 |
| US 2006025425 | A1 | 20060202 | US 2005-179458 | 20050712 |
| PRIORITY APPLN. INFO.: | | | US 2000-257492P | P 20001221 |
| | | | US 2001-38069 | A3 20011221 |
| | | | WO 2001-US50038 | W 20011221 |

OTHER SOURCE(S): MARPAT 137:47200
 GI



AB Title compds. I [W = N or CR3, X = N or CR4, Y = N or CR5, Z = N or CR6 with the provision that no more than two of W, X, Y and Z are N; Q = O or CR7R8; R1 = H, haloalkyl, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, etc.; R2 = nitrogen containing 5-7 membered (un)substituted heteroaryl or heterocycloalkyl ring with up to 4 heteroatoms independently selected from N, S, and O; R3, R4, R5 and R6 are independently selected from H, halo, OH, NO2, CN, (un)substituted alkyl, alkoxy, etc.] and there pharmaceutically acceptable salts are prepared and disclosed as selective GABAA receptor ligands. Thus, II was prepared in five steps from malonyl dichloride and Et vinyl ether with imidazole ring formation via cyclocondensation of 3-amino-4-ethylaminobenzonitrile with 1-(3-fluorophenyl)-5-carboxymethylpyrazole. The invention is particularly related to such compds. that bind with high selectivity and high affinity to the benzodiazepine site of GABAA receptors. Preferred compds. of the invention exhibit Ki values of < 100 nM for binding at the benzodiazepine site with more preferred compds. exhibiting Ki values of < 10 nM. This invention also relates to pharmaceutical compns. comprising such compds. and to the use of such compds. in treatment of certain central nervous system (CNS) diseases. This invention also relates to the use of I in combination with one or more other CNS agents to potentiate the effects of the other CNS agents. Addnl. this invention relates to the use such compds. as probes for the localization of GABAA receptors in tissue sections.

L15 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:786235 HCAPLUS
 DOCUMENT NUMBER: 134:86068
 TITLE: New Syntheses of the C,D-Ring Pyrromethenones of
 Phytochrome and Phycocyanin
 AUTHOR(S): Jacobi, Peter A.; **DeSimone, Robert W.**;
 Ghosh, Indranath; Guo, Jiasheng; Leung, Sam H.;
Pippin, Douglas
 CORPORATE SOURCE: Hall-Atwater Laboratories, Wesleyan University,
 Middletown, CT, 06459-0180, USA
 SOURCE: Journal of Organic Chemistry (2000), 65(25), 8478-8489
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134:86068
 GI



AB Pyrromethenone (I) (double bond), the C,D-ring segment of phytochrome, has been prepared in an efficient fashion employing three new strategies. Each of these has potential advantages for the synthesis of labeled material. Our first approach is related to the Gossauer synthesis, with the difference that strong alkali is avoided in the condensation of the C- and D-ring components (II) (R = CHO) and (III). The key silyloxypyrrole III was readily prepared on multigram scales beginning with inexpensive butyrolactone (IV). A second synthesis began with 2-acetylbutyrolactone. The key steps involved conversion of IV to the Z-enol triflate, followed by Pd(0)-catalyzed coupling with trimethylsilylacetylene, p-chlorophenylselenide ring opening, and finally, amidation to afford the ring-D synthon (Z)-4-ClC₆H₄SeCH₂CH₂C[=C(Me)C(=O)NH₂]CONH₂ (V) having the proper geometry and oxidation state for conversion to I. Sonogashira coupling of V with the iodopyrrole II (R = I) (VI), followed by oxidative elimination, and F⁻-induced 5-exo-dig cyclization of the resultant pyrroloalkyne (VII), then completed the synthesis. In similar fashion, we have also prepared pyrromethenone I (bond single) (VIII), the C,D-ring segment of phycocyanin.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que 118 nos

L1 STR
 L3 570 SEA FILE=REGISTRY SSS FUL L1
 L4 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
 L5 57 SEA FILE=HCAPLUS ABB=ON PLU=ON "DESIMONE R W"/AU OR "DESIMONE ROBERT"/AU OR ("DESIMONE ROBERT W"/AU OR "DESIMONE ROBERT WALTER JR"/AU)
 L6 18 SEA FILE=HCAPLUS ABB=ON PLU=ON "PIPPIN D A"/AU OR ("PIPPIN DOUGLAS"/AU OR "PIPPIN DOUGLAS A"/AU OR "PIPPIN DOUGLAS ANTHONY IRWIN"/AU)
 L7 26 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DARROW J W"/AU OR "DARROW JAMES W"/AU OR "DARROW JAMES WILLIAM"/AU)
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 2003

=> d ibib abs l18 1-40

L18 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:44034 HCAPLUS

DOCUMENT NUMBER: 140:264834

TITLE: Role of Cl⁻ co-transporters in the excitation produced by GABAA receptors in juvenile bovine adrenal chromaffin cells

AUTHOR(S): Xie, Z.; Currie, K. P. M.; Cahill, A. L.; Fox, A. P.

CORPORATE SOURCE: Department of Anesthesia and Critical Care, The University of Chicago, Chicago, IL, 60637, USA

SOURCE: Journal of Neurophysiology (2003), 90(6), 3828-3837

CODEN: JONEA4; ISSN: 0022-3077

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB GABA is the primary inhibitory neurotransmitter in the adult mammalian brain. However, in neonatal animals, activation of Cl⁻-permeable GABA receptors is excitatory and appears to depend on the expression of a Na⁺-K⁺-2Cl⁻ cotransporter (NKCC) that elevates intracellular Cl⁻ levels, leading to a depolarized Cl⁻ equilibrium potential (E_{Cl}). The change from excitation to inhibition appears to involve the expression of the K⁺/Cl⁻ co-transporter, KCC2, which lowers intracellular Cl⁻ levels resulting in a hyperpolarized E_{Cl}. In this study, the authors show that bovine chromaffin cells from 4- to 5-mo-old animals are excited by GABA. Activation of GABAA receptors depolarizes the cells, opens voltage-dependent Ca²⁺ channels, elevates [Ca²⁺]_i, and promotes the release of **catecholamines**. Blockade of voltage-dependent Ca²⁺ channels prevents the elevation of [Ca²⁺]_i by GABA. The extrapolated anion reversal potential in these cells is approx. -28 mV, indicating a resting intracellular anion concentration of approx. 50 mM. Expression of KCC2 protein was not detected in the juvenile chromaffin cells. In contrast, clear expression of NKCC1 was observed. Blockade of NKCC1 should reduce the intracellular Cl⁻ concentration and hyperpolarize E_{Cl}. Bumetanide, an NKCC1 blocker, reduced the elevation of [Ca²⁺]_i by GABA. In some cells, activation of GABAA receptors inhibits responses to excitatory neurotransmitters, even though GABA itself is depolarizing. Co-activation of cholinergic and GABAA receptors in chromaffin cells produced elevations in [Ca²⁺]_i that were comparable to those produced by cholinergic receptors alone. The authors' data showing the selective expression of chloride co-transporters and the resulting strongly depolarized anion reversal potential may help explain how activation of GABAA receptors causes sufficient excitation to elicit **catecholamine** release from

chromaffin cells.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:928895 HCAPLUS

DOCUMENT NUMBER: 140:145879

TITLE: Duloxetine (Cymbalta), a dual inhibitor of serotonin and norepinephrine reuptake

AUTHOR(S): Bymaster, F. P.; Beedle, E. E.; Findlay, J.; Gallagher, P. T.; Krushinski, J. H.; **Mitchell, S.**; Robertson, D. W.; Thompson, D. C.; Wallace, L.; Wong, D. T.

CORPORATE SOURCE: Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(24), 4477-4480

CODEN: BMCLE8; ISSN: 0960-894X

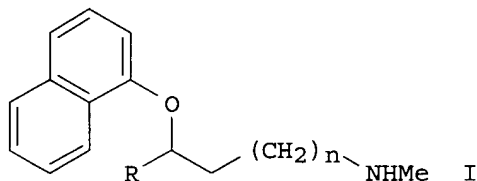
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:145879

GI



AB A series of naphthalenyloxy-substituted **amines** I ($n = 2 - 4$, $R = H$; $n = 1$, $R = H, Ph, 4-FC_6H_4, 2-MeOC_6H_4, 2-furyl, 2-thienyl, 2-thiazolyl$, etc.) has been prepared, and these compds. are demonstrated to be inhibitors of both serotonin and norepinephrine reuptake. One member of this series, duloxetine (Cymbalta), (S)-I ($n = 1$; $R = 2-thienyl$), has proven to be effective in clin. trials for the treatment of depression.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:58094 HCAPLUS

DOCUMENT NUMBER: 138:106720

TITLE: Preparation of heteroaryl substituted fused bicyclic heteroaryl compounds as benzodiazepine-GABAA receptor ligands and probes

INVENTOR(S): Hutchison, Alan; Maynard, George; Albaugh, Pamela; Xie, Linghong; Yuan, Jun; **Mitchell, Scott**; Singh, Vinod; Ghosh, Manuka; Li, Guiying; Liu, Nian

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 141 pp.

CODEN: PIXXD2

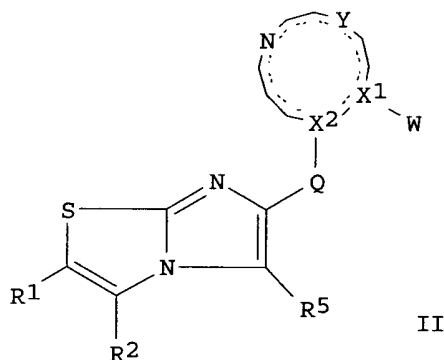
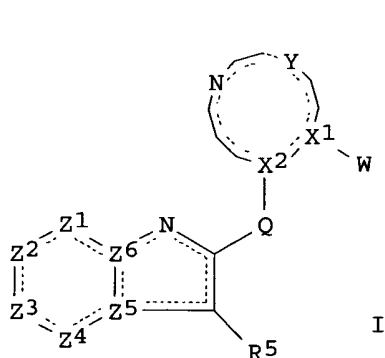
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|--------------|
| WO 2003006471 | A1 | 20030123 | WO 2002-US22130 | 20020712 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2453554 | AA | 20030123 | CA 2002-2453554 | 20020712 <-- |
| US 2003207885 | A1 | 20031106 | US 2002-194852 | 20020712 |
| US 6936617 | B2 | 20050830 | | |
| EP 1406906 | A1 | 20040414 | EP 2002-749983 | 20020712 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE | | | | |
| BR 2002011124 | A | 20040629 | BR 2002-11124 | 20020712 |
| CN 1553916 | A | 20041208 | CN 2002-816696 | 20020712 |
| JP 2005505518 | T2 | 20050224 | JP 2003-512241 | 20020712 |
| NZ 530992 | A | 20050624 | NZ 2002-530992 | 20020712 |
| US 2006014746 | A1 | 20060119 | US 2005-214345 | 20050829 |
| PRIORITY APPLN. INFO.: | | | US 2001-305533P | P 20010713 |
| | | | US 2002-194852 | A3 20020712 |
| | | | WO 2002-US22130 | W 20020712 |
| OTHER SOURCE(S): | | | MARPAT 138:106720 | |
| GI | | | | |



AB This invention relates to heteroaryl substituted fused bicyclic heteroaryl compds., such as heteroaryl-substituted **imidazopyridines**, **imidazopyrazines**, **imidazopyridazines**, **imidazopyrimidines**, and **imidazothiazoles**, which may be described by I or II (variables defined below; e.g. 5-ethyl-6-[[2-(6-fluoro-pyridin-2-yl)imidazol-1-yl]methyl]imidazo [2,1-b]thiazole). The invention particularly relates to such compds. that bind with high selectivity and high affinity to the benzodiazepine site of GABAA receptors. In a assay of GABAA receptor binding that dets. the displacement of 3H-Flumazenyl from rat cortical tissue in 0.05M Tris HCl

buffer at 4°, I or II exhibit K_i of 1-micromolar or less; preferred compds. exhibit K_i of 100 nanomolar or less; and more preferred compds. exhibit K_i of 10-nanomolar or less. This invention also relates to pharmaceutical compns. comprising such compds. and to the use of such compds. in treatment of certain central nervous system (CNS) diseases. Processes for preparing I and II are disclosed but not claimed; 13 example preps. are included. This invention also relates to the use of **benzimidazoles, pyridylimidazoles** and related I and II in combination with ≥ 1 other CNS agents to potentiate the effects of the other CNS agents. Addnl. this invention relates to the use of such compds. as probes for the localization of GABAA receptors in tissue sections (no data). For I: Z1 is N or CR1; Z2 is N or CR2; Z3 is N or CR3; Z4 is N or CR4; Z5 is N or C; Z6 is N or C; provided that no more than two of Z1-Z6 are N. R1, R2, R3, and R4 = (i) H, halogen, hydroxy, nitro, cyano, amino, haloalkyl, and haloalkoxy; (ii) alkyl, alkoxy, cycloalkyl, alkenyl, alkynyl, (cycloalkyl)alkyl, -NH(R10), -N(R10)(R11), hydroxyalkyl, aminoalkyl, (R10)NHalkyl, (R10)(R11)Nalkyl, alkanoyl, alkoxycarbonyl, alkylsulfonyl, (C1-C6)alkylsulfinyl, alkylthio, mono- and dialkylaminocarbonyl, heterocycloalkyl, aryl, and heteroaryl; (iii) -GRA (G is alkyl, -O-, -C(O)-, or -CH2-C(O)-, and RA is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl). (iv) -C(O)JRBRC (J is N, CH, or C-alkyl, and RB and RC = H, alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, (cycloalkyl)alkyl, heterocycloalkyl, aryl, arylalkyl, alkanoyl, heteroaryl, and mono and dialkylaminoalkyl, or RB and RC and the atom to which they are attached form a 4- to 10-membered monocyclic or bicyclic ring, comprising: a) 0-3 double bonds, and (b) 0-3 O, S, SO, SO2, or N-RD (RD is (1) hydrogen; or (2) Ar1, alkyl, cycloalkyl, heterocycloalkyl, or Ar1alkyl (Ar1 is aryl or heteroaryl)); and (v) -OC(O)RE, -C(O)NH2, -C(O)NHRE, -C(O)NRERF, -S(O)nRE, -S(O)nNH2, -S(O)nNHRE, -S(O)nNRERF, -NHC(O)RE, -C(:NRE)RF, -HC:N-OH, -HC:N(alkoxy), -HC:N(alkyl), -NREC(O)RF, -NHS(O)nRE, and -NRES(O)nRF (n is 0-2; RE and RF = alkyl, cycloalkyl, heterocycloalkyl, alkoxy, mono- and dialkylamino, aryl, and heteroaryl). R5 = (i) H, halogen, cyano, or haloalkyl; (ii) alkyl, cycloalkyl, (cycloalkyl)alkyl, each of which comprises 0-3 double bonds and/or = 0-3 triple bonds; or (iii) aryl, arylalkyl, heteroaryl, or heteroarylalkyl. Q = -C(R6)(R7), -N(alkyl)- or O (R6 and R7 = H, F, or alkyl); with the proviso that Q is not O when X2 is N; X1 and X2 = N, C or CH; Y is N, C, -CH-, -CH2-, or absent; and W = aryl or heteroaryl. For II, see the claims.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:889201 HCAPLUS

DOCUMENT NUMBER: 137:370091

TITLE: Preparation of 1-benzylimidazoles as glucagon-like peptide-1 (GLP-1) receptor ligands.

INVENTOR(S): He, Xiao-Shu; Zhang, Xiaoyan; Zhao, He; **Desimone, Robert**; Thurkauf, Andrew

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: U.S., 11 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|--------------|
| ----- | ---- | ----- | ----- | ----- |
| US 6482844 | B1 | 20021119 | US 2001-827565 | 20010406 <-- |

PRIORITY APPLN. INFO.:

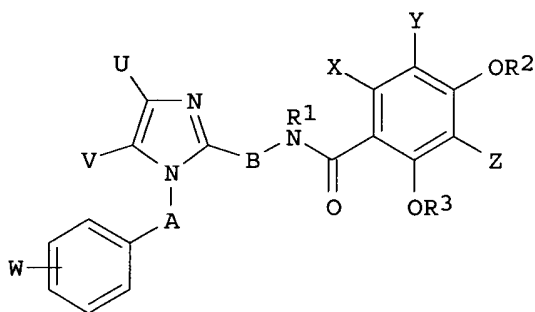
US 2000-195537P

P 20000407

OTHER SOURCE(S):

MARPAT 137:370091

GI



I

AB Title compds. [I; A B = C1-3 alkylene; R1 = C1-6 alkyl; R2, R3 = H, C1-6 alkyl; U, V = C1-6 alkyl, halo; X, Y, Z = H, C1-6 alkyl, CF3, C1-6 alkoxy, OCF3, halo, cyano; W = ≤3 of C1-6 alkyl, CF3, C1-6 alkoxy, OCF3, halo, OH, amino, cyano], were prepared as modulators of blood glucose levels and are useful for the treatment of diabetes, eating disorders, and obesity (no data). Thus, 1-[(2-chlorobenzyl)-4,5-dimethylimidazol-2-yl]methyl(3-methylbutyl)amine (preparation given), 2,4-dimethoxybenzoyl chloride, and Et3N were stirred overnight in CHCl3 to give N-(3-methylbutyl)-2,4-dimethoxy-N-[[1-(2-chlorophenylmethyl)-4,5-dimethyl-1H-imidazol-2-yl]methyl]benzamide.

REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:830255 HCAPLUS

DOCUMENT NUMBER: 137:325406

TITLE: Preparation of aminoalkyl-substituted pyridino[2,3-b]indole and pyrimidino[4,5-b]indole derivatives as CRF1 specific ligands

INVENTOR(S): Horvath, Raymond F.; Darrow, James W.; Maynard, George D.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 6,291,473.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

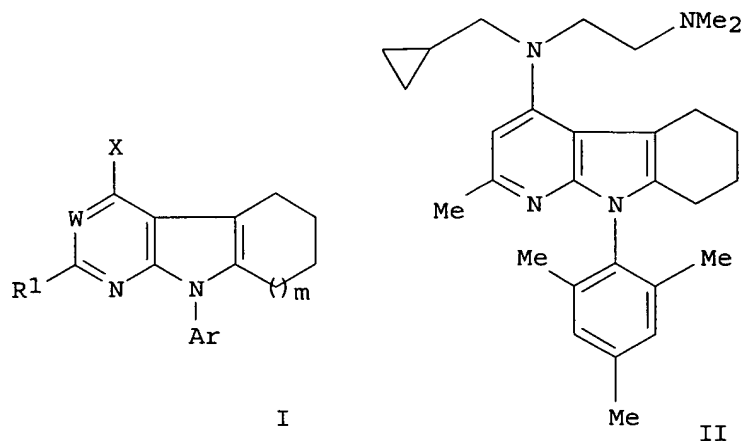
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| US 6472402 | B1 | 20021029 | US 1999-408613 | 19990930 <-- |
| US 6291473 | B1 | 20010918 | US 1999-283723 | 19990401 <-- |
| US 2003105117 | A1 | 20030605 | US 2002-228772 | 20020827 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-80410P | P 19980402 |
| | | | US 1999-283723 | A2 19990401 |
| | | | US 1999-408613 | A1 19990930 |

OTHER SOURCE(S): MARPAT 137:325406

GI



AB Title compds. I [Ar = Ph, naphthyl, pyridyl, pyrimidinyl, halo, CF₃, OH, amino, carboxamido, alkyl, alkoxy, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the tricyclic ring system is substituted; R₁ = H, halo, CF₃, alkyl; R₃ = H, alkyl; m = 0-2; X = substituted amino] were prepared For instance, 2-Amino-4,5,6,7-tetrahydro-1-phenyl-1H-indole-3-carbonitrile (preparation given) was subjected to the following sequence: i. 1,2-dichloroethane (DCE), 2-methoxypropene, pTsoH, reflux, 1 h; ii. DCE, c-C₃H₇COCl, (i-Pr)₂NEt, reflux; iv. THF, BH₃•SMe₂, reflux, 8 h; v. DCE, ClCOCH₂Cl, reflux, 4 h; vi. THF, BH₃•SMe₂, reflux, 1 h and vii. NMP, Me₂NH, 80°, 10 h (bomb) to afford II. Example compds. had IC₅₀ in the range of 0.5 nM to 10 μM for the CRF1 receptor. I are useful for the treatment of anxiety, depression, etc.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:466012 HCAPLUS

DOCUMENT NUMBER: 137:47228

TITLE: Preparation of spiro[isobenzofuran-1,4'-piperidin]-3-ones and 3H-spiroisobenzofuran-1,4'-piperidines as NPY5 receptor activity modulators

INVENTOR(S): Bakthavatchalam, Rajagopal; Blum, Charles A.; Brielmann, Harry L.; Darrow, James William; De Lombaert, Stephane; Hutchison, Alan; Tran, Jennifer; Zheng, Xiaozhang; Elliott, Richard Louis; Hammond, Marlys

PATENT ASSIGNEE(S): Neurogen Corporation, USA; Pfizer Inc.

SOURCE: PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

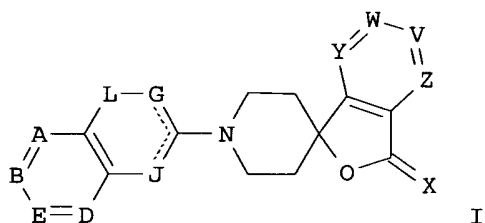
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
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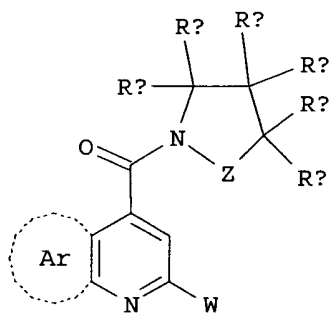
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|---|----|----------|------------------|--------------|
| WO 2002048152 | A2 | 20020620 | WO 2001-US47863 | 20011211 <-- |
| WO 2002048152 | A3 | 20030508 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002020276 | A5 | 20020624 | AU 2002-20276 | 20011211 <-- |
| US 2003036652 | A1 | 20030220 | US 2001-13846 | 20011211 <-- |
| US 6566367 | B2 | 20030520 | | |
| EP 1347982 | A2 | 20031001 | EP 2001-270536 | 20011211 |
| EP 1347982 | B1 | 20051116 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004520299 | T2 | 20040708 | JP 2002-549683 | 20011211 |
| BR 2001016113 | A | 20040803 | BR 2001-16113 | 20011211 |
| AT 310004 | E | 20051215 | AT 2001-270536 | 20011211 |
| US 2004072847 | A1 | 20040415 | US 2003-410648 | 20030409 |
| US 6943199 | B2 | 20050913 | | |
| US 2005033048 | A1 | 20050210 | US 2003-415457 | 20030815 |
| US 2006040964 | A1 | 20060223 | US 2005-183615 | 20050718 |
| PRIORITY APPLN. INFO.: | | | US 2000-254990P | P 20001212 |
| | | | US 2001-13846 | A3 20011211 |
| | | | WO 2001-US47863 | W 20011211 |
| | | | US 2003-410648 | A3 20030409 |
| OTHER SOURCE(S): | | | MARPAT 137:47228 | |
| GI | | | | |



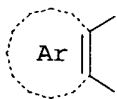
AB Title compds. [I; X = O, H₂; A, D, V, W, Y, Z independently = N, CR₁; R₁ = H, halo, OH, NH₂, NO₂, CN, CONH₂, COOH; B = N, CR₂; E = CR₃; R₂, R₃ independently = H, halo, OH, NH₂, NO₂, CN, CONH₂, COOH; G = N, NH; J = NH, N; L = bond, CO; dotted bond = single, double] capable of modulating NPY₅ receptor activity are prepared. Such compds. may be used to modulate ligand binding to NPY₅ receptors in vivo or in vitro, and are particularly useful in the treatment of a variety of disorders (e.g., eating disorders such as obesity or bulimia, psychiatric disorders, diabetes and cardiovascular disorders such as hypertension) in humans, domesticated companion animals and livestock animals. Pharmaceutical compns. and method for treating such disorders are provided, as are methods for using such compds. for detecting NPY₅ receptors.

L18 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:142664 HCAPLUS
 DOCUMENT NUMBER: 136:183713
 TITLE: Preparation of 2,4-substituted pyridine derivatives as agonists, antagonists or inverse agonists for GABAA brain receptors or their prodrugs
 INVENTOR(S): Cai, Guolin; Albaugh, Pamela; Yuan, Jun; Currie, Kevin S.; Hutchison, Alan
 PATENT ASSIGNEE(S): Neurogen Corporation, USA
 SOURCE: PCT Int. Appl., 110 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

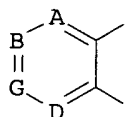
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|--------------|
| WO 2002014269 | A2 | 20020221 | WO 2001-US41757 | 20010816 <-- |
| WO 2002014269 | A3 | 20020808 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2418853 | AA | 20020221 | CA 2001-2418853 | 20010816 <-- |
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| US 6559163 | B2 | 20030506 | | |
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| EP 1337523 | B1 | 20051019 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001013300 | A | 20040113 | BR 2001-13300 | 20010816 |
| JP 2004506038 | T2 | 20040226 | JP 2002-519414 | 20010816 |
| AT 307127 | E | 20051115 | AT 2001-964614 | 20010816 |
| ES 2250464 | T3 | 20060416 | ES 2001-1964614 | 20010816 |
| US 2004048867 | A1 | 20040311 | US 2003-429107 | 20030502 |
| PRIORITY APPLN. INFO.: | | | US 2000-225552P | P 20000816 |
| | | | US 2001-931549 | A1 20010816 |
| | | | WO 2001-US41757 | W 20010816 |
| OTHER SOURCE(S): | | | MARPAT 136:183713 | |
| GI | | | | |



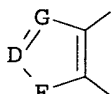
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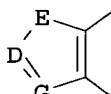
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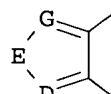
III



IV



V



VI

AB Disclosed are compds. (I; (R)-1-[[2-(3,4-difluorophenyl)-4-quinolinyl]carbonyl]-2-hydroxymethylpyrrolidine (1)) or pharmaceutically acceptable salts thereof wherein: II represents III-VI; A, B, D and G are N or CR1; E = O, S, NR5; Z = (CRaRb)_n (n = 0-2); and R1, R5, Ra, Rb, and W are defined herein. These compds. are agonists, antagonists or inverse agonists for GABAA brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABAA brain receptors and are therefore useful in the diagnosis and treatment of anxiety, depression, Down's syndrome, sleep and seizure disorders, overdose with benzodiazepine drugs and for enhancement of memory. Particularly preferred compds. have K_i values of <100 nM in a standard assay for GABAA binding affinity. Pharmaceutical compns., including packaged pharmaceutical compns., are further provided. 1 Are also useful as probes for the localization of GABAA receptors in tissue samples. Only the preparation of 1 is included, but >100 other compds. are specifically mentioned. Intermediate 2-(3,4-difluorophenyl)-4-quinoline carboxylic acid was prepared by heating a mixture of 2,3-indolinedione (0.03 mol), 3',4'-difluoroacetophenone (0.03 mol) and KOH (0.05 mol) in 1,4-dioxane (50 mL) at 105° for 48 h. The reaction solution was then cooled to room temperature and concentrated under reduced pressure. The residue was treated

with EtOAc and extracted with H₂O. The pH of the aqueous layer was adjusted to 5-6 with 1N HCl, the resulting solid was collected by vacuum filtration, washed with H₂O, and dried to give the intermediate (450 mg) as a yellow solid. A mixture of the intermediate (100 mg), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (220 mg) and (R)-(-)-pyrrolidinemethanol (0.1 mL) in 1 mL of DMF was stirred at room temperature for 18 h. The mixture was added to saturated aqueous NaHCO₃ solution and extracted

three times with EtOAc. The combined EtOAc layers were washed with brine and H₂O, dried over Na₂SO₄, filtered and concentrated to afford a foam. The foam containing 1 was purified by preparative silica gel thin layer chromatog., using 10% MeOH in CH₂Cl₂ as the developing solvent.

L18 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:123169 HCAPLUS

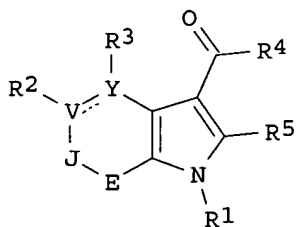
DOCUMENT NUMBER: 136:183807

TITLE: Heterocyclic annulated carboxylpyrroles as ligands for altering the signal transducing activity of GABAA

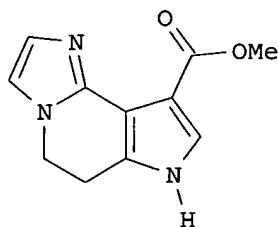
receptors
 INVENTOR(S): Maynard, George; Yohannes, Daniel; Yuan, Jun; Xie, Linghong; Ghosh, Manuka; Luke, George P.; Liu, Xiaojun; Nagel, Arthur Adam; Vincent, Lawrence Albert; Currie, Kevin S.; Wang, Zhe-Qing; Lee, Kyungae
 PATENT ASSIGNEE(S): Neurogen Corporation, USA; Pfizer, Inc.; et al.
 SOURCE: PCT Int. Appl., 397 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2002012442 | A2 | 20020214 | WO 2001-US41572 | 20010806 <-- |
| WO 2002012442 | A3 | 20030501 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2420967 | AA | 20020214 | CA 2001-2420967 | 20010806 <-- |
| US 2003105081 | A1 | 20030605 | US 2001-924174 | 20010806 <-- |
| US 6653471 | B2 | 20031125 | | |
| EP 1325006 | A2 | 20030709 | EP 2001-964561 | 20010806 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004505942 | T2 | 20040226 | JP 2002-517733 | 20010806 |
| BR 2001013120 | A | 20040622 | BR 2001-13120 | 20010806 |
| US 2004110778 | A1 | 20040610 | US 2003-670077 | 20030923 |
| US 6949562 | B2 | 20050927 | | |
| PRIORITY APPLN. INFO.: | | | US 2000-223669P | P 20000807 |
| | | | US 2001-924174 | A1 20010806 |
| | | | WO 2001-US41572 | W 20010806 |

OTHER SOURCE(S): MARPAT 136:183807
 GI



I



II

AB Title compds. I [R1 = H, OH, amino, alkylamino, alkyl or alkoxy; R2R3 together with the atom they are attached to form (un)substituted heterocyclic ring; R4 = GQ(CH2)nW(CH2)mZ {wherein G = O or NH; Q = (un)saturated carbocyclic or heterocyclic group where each group has from 1-3 rings; W = bond, O, NH, S, etc.; Z = H, OH, hydroxyalkyl, alkoxy, amino,

etc; n = 0, 1, 2 or 3 and m = 0, 1, 2 or 3}; R5 = R1, halo; Y = C or CH; V = N, C, or CH; J = (CR6R7)d where d = 0 or 1 and R6 and R7 together form a carbonyl group or R6 and R7 are independently H, NO₂, CN, amino, aryl, etc.; E = (un)saturated-(un)substituted alkyl or heteroalkyl chain of 0-3 atoms] and the pharmaceutically acceptable salts thereof are prepared and disclosed as ligands for GABAA receptors. Thus, II was prepared in 10 steps from p-nitrophenylethylamine with each heterocyclic ring being formed via cyclocondensation reactions. I are highly selective agonists, antagonists or inverse agonists for GABAA brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABAA brain receptor (no data). As agonists, antagonists or inverse agonists for GABAA brain receptors the compds. of the invention may be useful for treating anxiety, depression, sleep disorders, or Alzheimer's dementia.

L18 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:663247 HCAPLUS

DOCUMENT NUMBER: 136:197930

TITLE: **Fructosamine** concentration and resistance to natural, predominantly *Teladorsagia circumcincta* infection

AUTHOR(S): Stear, M. J.; Eckersall, P. D.; Graham, P. A.; McKellar, Q. A.; **Mitchell, S.**; Bishop, S. C.

CORPORATE SOURCE: Glasgow University Veterinary School, Glasgow, G61 1QH, UK

SOURCE: Parasitology (2001), 123(2), 211-218

CODEN: PARAAE; ISSN: 0031-1820

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Fructosamine** concns. reflect protein status and because infection with *Teladorsagia circumcincta* can induce a relative protein deficiency, we examined the usefulness of **fructosamine** concns. as markers of the intensity of infection in naturally infected lambs. **Fructosamine** concentration was a heritable trait and variation in **fructosamine** concns. was associated with differences in body weight, and a variety of parasitol. variables; animals with increased **fructosamine** concns. grew more quickly, had increased fecal egg counts in one of the three study years, had decreased pepsinogen concns. and decreased IgA activity against 4th-stage larvae of *T. circumcincta*. **Fructosamine** concns. were also associated with variation in the subsequent acquisition of nematodes and in the length of adult female *T. circumcincta*; lambs with increased **fructosamine** concns. had fewer nematodes but the mean length of adult female *T. circumcincta* was longer. Therefore **fructosamine** concns. are potentially useful indicators of the severity of nematode infection and may predict magnitude of subsequent infection.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:640102 HCAPLUS

TITLE: Structure-activity relationships within a series of pyrazolopyrimidine NPY-Y1 receptor antagonists

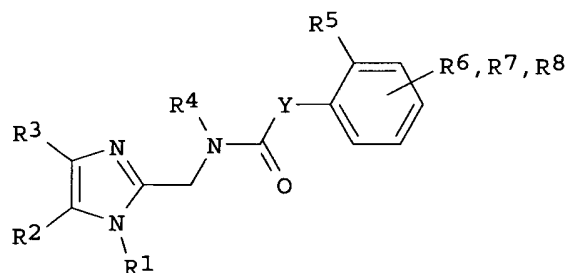
AUTHOR(S): Griffith, David A.; Blum, Charles A.; Carpino, Philip A.; Cassella, James; **Darrow, James W.**; De Lombaert, Stephane; Hargrove, Diane M.; Hickman, M. Anne; Mack, Christine M.; Maurer, Tristan S.; Sanders, Martin J.; Ashton, Michael A.; Giangliordano, Mark; He, Ping; Inthavongsay, John K.; Klade, Lee E.; Lebel, Wesley S.; Martin, Kelly A.; Regan, Christa; Rose,

CORPORATE SOURCE: Colin R.; Tran, Jennifer; Vage, Chandra
 SOURCE: Pfizer Inc, Groton, CT, 06340, USA
 Abstracts of Papers, 222nd ACS National Meeting,
 Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-283. American Chemical Society:
 Washington, D. C.
 CODEN: 69BUZP
 DOCUMENT TYPE: Conference; Meeting Abstract
 LANGUAGE: English
 AB Neuropeptide Y is a potent orexigenic agent that has been proposed to stimulate food-intake via the Y1 and Y5 receptor subtypes (Y1-R and Y5-R). We were interested in exploring the role of the Y1-R in both NPY-stimulated and natural feeding. Using high throughput screening and directed synthesis, we identified N-[3-(2,6-dichloro-4-methoxyphenyl)-2,5-dimethylpyrazolo[1,5-a]pyrimidin-7-yl]-N'-(tetrahydropyran-4-yl)-ethane-1,2-diamine (CP-671906-01) as a potent, selective, non-peptidic NPY-Y1 receptor antagonist [SK-N-MC Ki=4 nM; rabbit vas deferens Kb=26 nM; 100% inhibition of NPY-induced increase in blood pressure in rats at 3 mg/kg, iv]. Herein we report the structure-activity and structure-pharmacokinetic relationships of a series of pyrazolopyrimidine NPY antagonists and describe efforts to improve CNS and CSF exposures. Several compds. were identified that inhibited food intake, but high doses and exposure levels were required. We could not exclude the possibility that the observed anorectic effects were due to non-specific mechanisms.

L18 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:581850 HCAPLUS
 DOCUMENT NUMBER: 135:152807
 TITLE: Preparation of substituted **imidazoles** as selective modulators of bradykinin B2 receptors
 INVENTOR(S): Rachwal, Stanislaw; Hutchison, Alan; Shaw, Kenneth; Maynard, George D.; He, Xiao-Shu; **Desimone, Robert**; Hodgetts, Kevin J.
 PATENT ASSIGNEE(S): Neurogen Corporation, USA
 SOURCE: PCT Int. Appl., 117 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|--------------|
| ----- | ---- | ----- | ----- | ----- |
| WO 2001056995 | A1 | 20010809 | WO 2001-US1618 | 20010117 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002115693 | A1 | 20020822 | US 2001-764805 | 20010117 <-- |
| US 6509366 | B2 | 20030121 | | |
| US 2003229076 | A1 | 20031211 | US 2002-244180 | 20020916 |
| PRIORITY APPLN. INFO.: | | | US 2000-176869P | P 20000118 |
| | | | US 2001-764805 | A1 20010117 |
| OTHER SOURCE(S): | | MARPAT 135:152807 | | |
| GI | | | | |



AB The title compds. [I; R1 = (un)substituted aralkyl, heteroarylalkyl, allyl; R2, R3 = halo, CF3, alkoxy, etc.; R2 and R3 may be taken together to form a carbocyclic or heterocyclic saturated ring; R4 = alkyl; R5 = halo, CF3; R6-R8 = H, CF3, CN, etc.; Y = a bond, CH2] which are modulators of bradykinin B2 receptors, were prepared. E.g., a multi-step synthesis of I [R1 = 2-ClC6H4CH2; R2, R3 = Me; R4 = 3-methylbutyl; R5 = Cl; R6 = 3-OMe; R7 = 4-OMe; R8 = H; Y = a bond] was given. The compds. I are useful in the diagnosis and treatment of renal diseases, heart failure, hypertension, Meniere's disease, vaginal inflammation and pain, peripheral circulatory disorders, climacteric disturbance, retinobulbar disorders, circulatory disorders, myocardial ischemia, myocardial infarction, postmyocardial infarction syndrome, angina pectoris, restenosis after percutaneous transluminal coronary angioplasty, hepatitis, liver cirrhosis, pancreatitis, ileus, diabetes, diabetic complications, male infertility, glaucoma, pain, asthma, and rhinitis, and for the increase of permeability of the blood-brain barrier or the blood-brain-tumor barrier.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:247336 HCAPLUS

DOCUMENT NUMBER: 134:280866

TITLE: Preparation of certain alkylene diamine
-substituted pyrazolo[1,5-a]-1,5-pyrimidines and
pyrazolo[1,5-a]-1,3,5-triazines as selective
modulators of NPY1 receptors

INVENTOR(S): Darrow, James W.; De Lombaert, Stephane;
Blum, Charles; Tran, Jennifer; Giangioridano, Mark;
Griffith, David Andrew; Carpino, Philip Albert

PATENT ASSIGNEE(S): Neurogen Corporation, USA; Pfizer Inc.; De Lombaert,
Stephane

SOURCE: PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| WO 2001023387 | A2 | 20010405 | WO 2000-US26887 | 20000929 <-- |
| WO 2001023387 | A3 | 20020124 | | |

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CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

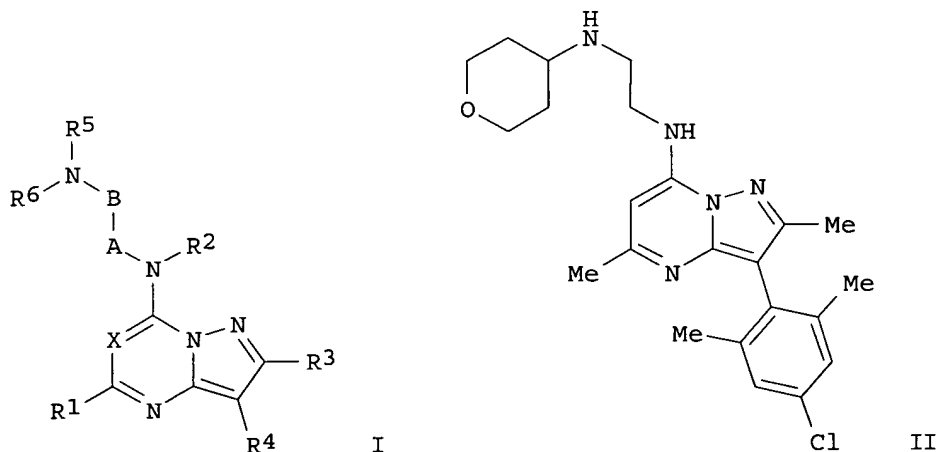
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|--|----|----------|-----------------|--------------|
| CA 2379585 | AA | 20010405 | CA 2000-2379585 | 20000929 <-- |
| US 6372743 | B1 | 20020416 | US 2000-676970 | 20000929 <-- |
| EP 1218379 | A2 | 20020703 | EP 2000-967134 | 20000929 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003510325 | T2 | 20030318 | JP 2001-526539 | 20000929 <-- |
| US 2003069246 | A1 | 20030410 | US 2002-83245 | 20020225 <-- |
| BG 106506 | A | 20021229 | BG 2002-106506 | 20020311 <-- |
| NO 2002001356 | A | 20020523 | NO 2002-1356 | 20020319 <-- |
| ZA 2002002519 | A | 20031128 | ZA 2002-2519 | 20020328 |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|----------|
| US 1999-156869P | P | 19990930 |
| US 2000-676970 | A1 | 20000929 |
| WO 2000-US26887 | W | 20000929 |

OTHER SOURCE(S):
GI

MARPAT 134:280866



AB The title compds. [I; X = N, CR14; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl which optionally forms (un)substituted aminocarbocycle or aminoheterocycle with A and B, etc.; R2 and R6 with 2 N atoms to which they are bound, form (un)substituted aminoheterocycle; R2 and A form (un)substituted aminocarbocycle, aminoheterocycle; A, B = (un)substituted alkyl; A and B form (un)substituted carbocycle; B and R6 form (un)substituted aminocarbocycle; R3 = H, alkyl, cycloalkyl, etc.; R4 = (un)substituted aryl, heteroaryl; R5 = (un)substituted (cycloalkyl)alkyl, alkenyl, alkynyl, etc.; R6 = H, alkyl, cycloalkyl, etc.; R14 = H, alkyl, etc.] which are selective modulators of NPY1 receptors, and are useful in the treatment of a number of CNS disorders, metabolic disorders, and peripheral disorders, particularly eating disorders and hypertension, were prepared E.g., a multi-step synthesis of the pyrazolo[1,5-a]pyrimidine II, was described. The NPY1 binding affinity for the compds. I, expressed as a Ki value, ranges from 0.1 nM to 10 µM. Compds. I are also useful as probes for the localization of NPY1 receptors and as stds. in assays for

NPY1 receptor binding. Methods of using the compds. I in receptor localization studies are given.

L18 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:172615 HCAPLUS
 DOCUMENT NUMBER: 134:353524
 TITLE: Solid-Phase Synthesis of O-Linked Glycopeptide Analogues of Enkephalin
 AUTHOR(S): **Mitchell, Scott A.**; Pratt, Matt R.; Hruby, Victor J.; Polt, Robin
 CORPORATE SOURCE: Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA
 SOURCE: Journal of Organic Chemistry (2001), 66(7), 2327-2342
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134:353524

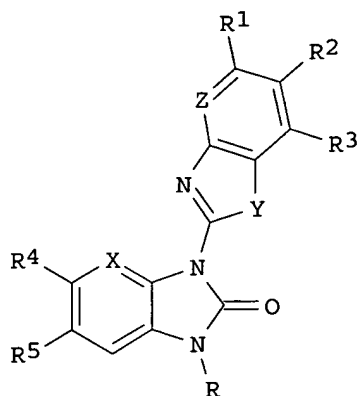
AB The synthesis of 18 N- α -Fmoc-amino acid glycosides for solid-phase glycopeptide assembly is reported. The glycosides were synthesized either from the corresponding O'Donnell Schiff bases or from N- α -Fmoc-amino protected serine or threonine and the appropriate glycosyl bromide using Hanessian's modification of the Koenigs-Knorr reaction. Reaction rates of D-glycosyl bromides (e.g., acetobromoglucose) with the L- and D-forms of serine and threonine are distinctly different and can be rationalized in terms of the steric interactions within the two types of diastereomeric transition states for the D/L and D/D reactant pairs. The N- α -Fmoc-protected glycosides [monosaccharides Xyl, Glc, Gal, Man, GlcNAc, and GalNAc; disaccharides Gal- β (1-4)-Glc (lactose), Glc- β (1-4)-Glc (cellobiose), and Gal- α (1-6)-Glc (melibiose)] were incorporated into 22 enkephalin glycopeptide analogs. These peptide opiates bearing the pharmacophore H-Tyr-c[DCys-Gly-Phe-DCys]- were designed to probe the significance of the glycoside moiety and the carbohydrate-peptide linkage region in blood-brain barrier (BBB) transport, opiate receptor binding, and analgesia (no data).

REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

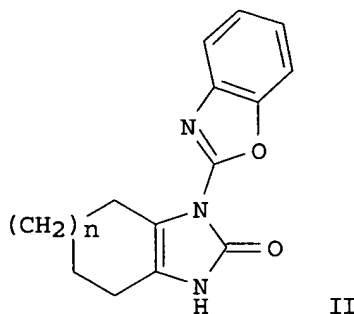
L18 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:853636 HCAPLUS
 DOCUMENT NUMBER: 134:178498
 TITLE: Substituted 3-(2-benzoxazolyl)-**benzimidazol**-2-(1H)-ones: A new class of GABAA brain receptor ligands
 AUTHOR(S): **DeSimone, R. W.**; Blum, C. A.
 CORPORATE SOURCE: Neurogen Corporation, Branford, CT, 06405, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2723-2726
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134:178498

GI



I



II

AB A novel class of potent benzodiazepine receptor (BZR) ligands I (R = H, Me; X = CH, N; Y = O, S; Z = CH, N; R1, R2 = H, F, MeO; R3, R4, R5 = H, F) and II (n = 1, 2), has been designed and synthesized aided by mol. modeling of known benzodiazepine ligands such as CGS-8216 and the use of known pharmacophore models. The structure-activity relationship was studied.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:814465 HCAPLUS

DOCUMENT NUMBER: 133:350153

TITLE: Preparation of substituted 4-oxo-quinoline-3-carboxamides as GABA brain receptor ligands

INVENTOR(S): Albaugh, Pamela A.; Currie, Kevin S.; Rosewater, Daniel; Cai, Goulin

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

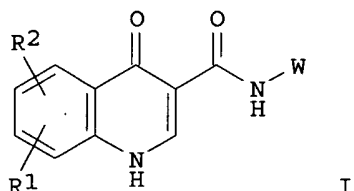
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2000068202 | A1 | 20001116 | WO 2000-US12096 | 20000505 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2371472 | AA | 20001116 | CA 2000-2371472 | 20000505 <-- |
| BR 2000010308 | A | 20020108 | BR 2000-10308 | 20000505 <-- |
| EP 1177177 | A1 | 20020206 | EP 2000-930341 | 20000505 <-- |
| EP 1177177 | B1 | 20050223 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 6413956 | B1 | 20020702 | US 2000-565529 | 20000505 <-- |

JP 2002544197 T2 20021224 JP 2000-617182 20000505 <--
 AT 289593 E 20050315 AT 2000-930341 20000505
 ES 2235883 T3 20050716 ES 2000-930341 20000505
 PRIORITY APPLN. INFO.: US 1999-132940P P 19990506
 WO 2000-US12096 W 20000505
 OTHER SOURCE(S): MARPAT 133:350153
 GI



AB The title compds. [I; R1, R2 = H, halo, alkyl, etc.; W = H, (un)substituted 3-7 membered cycloalkyl where up to two of the members are optionally heteroatoms selected from O and N atoms, (un)substituted alkyl] and their pharmaceutically acceptable salts which are highly selective agonists, antagonists or inverse agonists for GABAA brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABAA brain receptors, and are therefore useful in the diagnosis and treatment of anxiety, depression, Down Syndrome, sleep and seizure disorders, overdose with benzodiazepine drugs and for enhancement of memory, were prepared Thus, treating a solution of 4-oxo-1,4-dihydro-quinoline-3-carboxylic acid and Et3N in THF/DMF with Et chloroformate followed by addition of **tetrahydrofurfurylamine** afforded I [R1, R2 = H; W = tetrahydrofurfuryl]. The compds. I are effective at 0.1-140 mg/kg/day. The compds. I are also useful as probes for the localization of GABAA receptors in tissue samples.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:806616 HCAPLUS

DOCUMENT NUMBER: 133:350243

TITLE: Preparation of aminoalkyl substituted 9H-pyrido[2,3-b]indoles and 9H-pyrimido[4,5-b]indoles as CRF1 and neuropeptide Y1 receptors antagonists

INVENTOR(S): Horvath, Raymond F.; Darrow, James W.; Maynard, George D.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: U.S., 28 pp.
 CODEN: USXXAM

DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

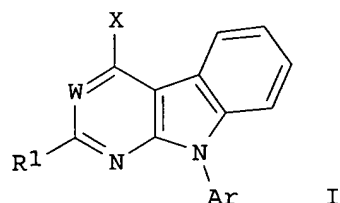
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| US 6147085 | A | 20001114 | US 1999-283409 | 19990401 <-- |
| JP 2002510688 | T2 | 20020409 | JP 2000-542321 | 19990401 <-- |
| US 6362186 | B1 | 20020326 | US 2000-707387 | 20001106 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-80451P | P 19980402 |
| | | | US 1999-283409 | A1 19990401 |

WO 1999-US7254

W 19990401

OTHER SOURCE(S) :
GI

MARPAT 133:350243



AB The title compds. [I; Ar = substituted Ph; R1 = H, halo, CF₃, etc.; W = N, CH, C(alkyl); X = disubstituted NH₂, piperazino, 4-triazolyl, etc.] which are (1) antagonists at CRF1 receptors and are, therefore, useful in the diagnosis and treatment of stress related disorders such as post traumatic stress disorder (PTSD) as well as depression, headache and anxiety, and (2) are neuropeptide Y1 receptor antagonists, and are therefore useful in the treatment of a variety of clin. conditions which are characterized by the presence of an excess of neuropeptide Y, were prepared E.g., a multi-step synthesis of I [W = CH; Ar = 2,4,6-Me₃C₆H₂; R1 = Me; X = N-(2-pyrrolidinoethyl)-N-(cyclopropylmethyl)amino] was given. The binding affinities for the compds. I towards the CRF1 receptor and towards the NPY1 receptor were expressed as IC₅₀ values and were less than 10 μM.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:785902 HCAPLUS

DOCUMENT NUMBER: 133:335225

TITLE: Substituted 4-oxo-naphthyridine-3-carboxamides: GABA brain receptor ligands

INVENTOR(S): Albaugh, Pamela A.; Desimone, Robert W.;
Liu, Gang

PATENT ASSIGNEE(S): Neurogen Corp., USA

SOURCE: U.S., 27 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

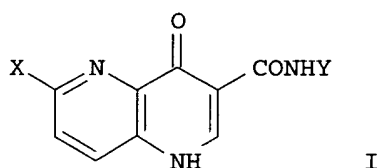
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|--------------|
| US 6143760 | A | 20001107 | US 1998-139456 | 19980825 <-- |
| ZA 9807957 | A | 20000322 | ZA 1998-7957 | 19980901 <-- |
| US 6399604 | B1 | 20020604 | US 2000-634093 | 20000808 <-- |
| US 2002156280 | A1 | 20021024 | US 2002-114743 | 20020402 <-- |
| US 6646124 | B2 | 20031111 | | |
| PRIORITY APPLN. INFO.: | | | US 1997-56799P | P 19970825 |
| | | | US 1998-139456 | A1 19980825 |
| | | | US 2000-634093 | A1 20000808 |

OTHER SOURCE(S) : MARPAT 133:335225

GI



AB The present invention encompasses substituted 4-oxo-naphthyridine-3-carboxamides I or the pharmaceutically acceptable nontoxic salts of I (X = H, halogen, (un)substituted alkyl, (un)substituted alkoxy or amino; and Y is (un)substituted alkyl, aryl, or heteroaryl). I are highly selective agonists, antagonists or inverse agonists for GABA_A brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABA_A brain receptors. I are useful in the diagnosis and treatment of anxiety, Down Syndrome, sleep, cognitive and seizure disorders, and overdose with benzodiazepine drugs and for enhancement of alertness.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:725632 HCAPLUS

DOCUMENT NUMBER: 133:296433

TITLE: Preparation of aryl and heteroaryl fused aminoalkyl-imidazole derivatives as selective modulators of GABA_A receptors

INVENTOR(S): Desimone, Robert W.; Hutchison, Alan; Shaw, Kenneth; Rosewater, Daniel L.

PATENT ASSIGNEE(S): Neurogen Corp., USA

SOURCE: PCT Int. Appl., 261 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

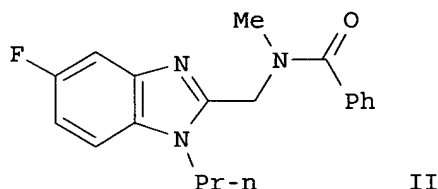
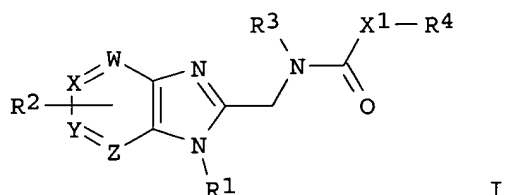
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|--------------|
| WO 2000059905 | A1 | 20001012 | WO 2000-US8610 | 20000331 <-- |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2369557 | AA | 20001012 | CA 2000-2369557 | 20000331 <-- |
| EP 1165557 | A1 | 20020102 | EP 2000-919975 | 20000331 <-- |
| EP 1165557 | B1 | 20040929 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| US 6380210 | B1 | 20020430 | US 2000-540454 | 20000331 <-- |
| JP 2002541151 | T2 | 20021203 | JP 2000-609416 | 20000331 <-- |
| US 6627624 | B1 | 20030930 | US 2000-541797 | 20000331 |
| AT 277927 | E | 20041015 | AT 2000-919975 | 20000331 |
| ES 2226812 | T3 | 20050401 | ES 2000-919975 | 20000331 |
| US 2003092912 | A1 | 20030515 | US 2002-115361 | 20020403 <-- |

| | | | | |
|------------------------|----|-------------------|-----------------|-------------|
| US 2004023993 | A1 | 20040205 | US 2003-609941 | 20030630 |
| US 6972293 | B2 | 20051206 | | |
| PRIORITY APPLN. INFO.: | | | US 1999-127526P | P 19990402 |
| | | | US 1999-285357 | A 19990402 |
| | | | US 2000-540454 | A1 20000331 |
| | | | WO 2000-US8610 | W 20000331 |
| | | | US 2002-115361 | B1 20020403 |
| OTHER SOURCE(S): | | MARPAT 133:296433 | | |
| GI | | | | |



AB Novel aryl or heteroaryl fused aminoalkyl-**imidazoles** I [W or X or Y or Z = N or CH with not more than two as N; X1 = bond, CH2, CHCH; R1 = Ph, alkyl, cyclopentyl, cyclohexyl, PhCH2, 3-FC6H4CH2, cyclopropylmethyl; R2 = H, OH, (un)substituted alkyl or alkoxy {substituents selected from amino, alkylamino, N attached heterocycloalkyl}, O(CH2)nCO2R5 {n = 1-4; R5 = H, alkyl}, NR5COR6 {R6 = H, alkyl}, COR5, CONR5R6, CO2R5, N-attached 5-, 6-, 7-membered heterocycle, N-attached amino derivs., etc.; R3 = alkyl, allyl, cyclopropylmethyl, cyclopentyl, (un)substituted benzyl {substituents selected from halo, NO2, CF3, OCF3, CN, OH, (un)substituted alkyl or alkoxy {substituents defined as above}, O(CH2)nCO2R5 {n = 1-4; R5 = H, alkyl}, NR5COR6 {R6 = H, alkyl}, COR5, CONR5R6, CO2R5, N-attached 5-, 6-, 7-membered heterocycle, SO2R5, NHSO2R5, SO2NHR5, SO2NHCOR5, CONHSO2R5, O(CH2)nCO2R7 {n = 1-4; R7 = SO2R5, NHSO2R5, SO2NHR5, SO2NHCOR5, CONHSO2R5}, tetrazole, triazole, **imidazole**, thiazole, oxazole, thiophene, pyridyl; R4 = (un)substituted benzene, furan, thiophene, thiazole or oxazole {substituents selected from (un)substituted-alkyl, -alkoxy {substituents defined as above}}, O(CH2)nCO2R5 {n = 1-4; R5 = H, alkyl}, NR5COR6 {R6 = H, alkyl}, COR5, CONR5R6, CO2R5, N-attached 5-, 6-, 7-membered heterocycle, fused 1,3-dioxolene], or the pharmaceutically acceptable non-toxic salts thereof, are prepared Thus, **imidazole** II was prepared by cyclocondensation of the corresponding N-propylfluoro-1,2-benzenediamine with Et chloroacetimidate hydrochloride followed by amination and benzoylation. The disclosed compds. are highly selective agonists, antagonists or inverse agonists (no data) for GABA_A brain

receptors, or prodrugs of such. The compds. are therefore useful in the diagnosis and treatment of anxiety, Down syndrome, sleep, cognitive and seizure disorders, depression, or overdose with benzodiazepine drugs, and for enhancement of memory and alertness.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:725616 HCAPLUS

DOCUMENT NUMBER: 133:296432

TITLE: Preparation of aryl and heteroaryl fused aminoalkyl-imidazoles as antidiabetics

INVENTOR(S): Desimone, Robert W.; Hutchison, Alan

PATENT ASSIGNEE(S): Neurogen Corp., USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

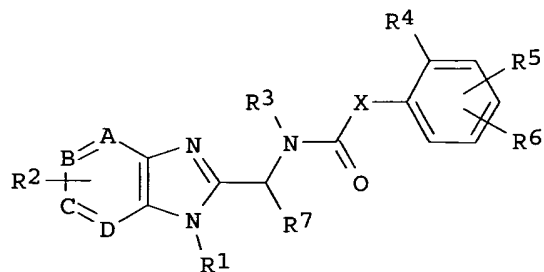
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2000059887 | A1 | 20001012 | WO 2000-US8569 | 20000331 <-- |
| W: | | | | |
| AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: | | | | |
| GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2369549 | AA | 20001012 | CA 2000-2369549 | 20000331 <-- |
| US 6271241 | B1 | 20010807 | US 2000-539835 | 20000331 <-- |
| EP 1165519 | A1 | 20020102 | EP 2000-919947 | 20000331 <-- |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002541146 | T2 | 20021203 | JP 2000-609399 | 20000331 <-- |
| US 2002082425 | A1 | 20020627 | US 2001-918292 | 20010730 <-- |
| PRIORITY APPLN. INFO.: | | | US 1999-127656P | P 19990402 |
| | | | US 1999-285415 | A 19990402 |
| | | | US 2000-539835 | A1 20000331 |
| | | | WO 2000-US8569 | W 20000331 |

OTHER SOURCE(S): MARPAT 133:296432

GI



I

AB The title compds. [I; R7 = H, alkyl; when R7 = H, R1 = (un)substituted 2-, 3-, 4-picolyl, CH2Ph; when R7 = alkyl, R1 = alkyl, cyclopentyl, cyclopropylmethyl; R2 = OH, alkyl, alkoxy, etc.; R3 = alkyl; R4 = alkoxy, Me (when R1, R7 = alkyl); R5, R6 = H, halo, alkyl, etc.; X = a bond, CH2O, CH:CH; A, B, C, D = CH, N; with the proviso that not more than two of A-D = N], useful in treatment of obesity and diabetes, were prepared E.g., a multi-step synthesis of I [R1 = 2-MeC6H4CH2; R2 = H; R3 = isoamyl; R4 = OMe; R5 = 4-OMe; R6, R7 = H; X = a bond; A-D = CH] was given. Compds. I are effective at 0.1-140 mg/kg/day. The invention also provides labeled probes for the localization of cellular receptors such as GLP-1 that are involved in the modulation of blood glucose levels.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:725615 HCAPLUS

DOCUMENT NUMBER: 133:296431

TITLE: Preparation of aryl and heteroaryl fused aminoalkyl-imidazoles as selective modulators of bradykinin B2 receptors

INVENTOR(S): Desimone, Robert W.; Hutchison, Alan; Shaw, Kenneth; Maynard, George D.; Peterson, John M.; Lew, Richard; Brielmann, Harry L.

PATENT ASSIGNEE(S): Neurogen Corp., USA

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

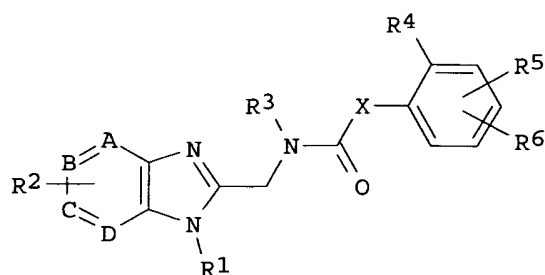
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|--------------|
| WO 2000059886 | A2 | 20001012 | WO 2000-US8568 | 20000331 <-- |
| WO 2000059886 | A3 | 20010913 | | |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2369544 | AA | 20001012 | CA 2000-2369544 | 20000331 <-- |
| EP 1165518 | A2 | 20020102 | EP 2000-919946 | 20000331 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| US 6358949 | B1 | 20020319 | US 2000-540580 | 20000331 <-- |
| JP 2002541145 | T2 | 20021203 | JP 2000-609398 | 20000331 <-- |
| US 2002151550 | A1 | 20021017 | US 2002-100697 | 20020318 <-- |
| PRIORITY APPLN. INFO.: | | | US 1999-127505P | P 19990402 |
| | | | US 1999-285327 | A 19990402 |
| | | | US 2000-540580 | A1 20000331 |
| | | | WO 2000-US8568 | W 20000331 |

OTHER SOURCE(S): MARPAT 133:296431

GI



AB The title compds. [I; A, B, C, D = N, CH; X = a bond, (un)substituted CH₂; R₁ = alkenyl, (un)substituted alkyl; R₂ = H, OH, halo, etc.; R₃ = alkyl; R₄ = halo, CF₃; R₅, R₆ = H, CF₃, OCF₃, etc.; R₄ and R₅ together with the carbon atoms to which they are attached form (un)substituted 5-6 membered aryl], useful in the diagnosis and treatment of renal diseases, heart failure, hypertension, Meniere's disease, vaginal inflammation and pain, peripheral circulatory disorders, climacteric disturbance, retinochoroidal circulatory disorders, myocardial ischemia, myocardial infarction, postmyocardial infarction syndrome, angina pectoris, restenosis after percutaneous transluminal coronary angioplasty, hepatitis, liver cirrhosis, pancreatitis, ileus, diabetes, diabetic complications, male infertility or glaucoma, or for the increase of permeability of blood-brain barrier, pain, asthma, and rhinitis (no data), were prepared E.g., a multi-step synthesis of I [A-D = CH; X = a bond; R₁ = 2-MeOC₆H₄CH₂; R₂ = H; R₃ = 3-MeBu; R₄ = Cl; R₅ = 3-MeO; R₆ = 4-MeO] was given. Compds. I are effective at 0.1-140 mg/kg/day.

L18 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:769540 HCAPLUS

DOCUMENT NUMBER: 132:47006

TITLE: The response of human glioma cell lines to low-dose radiation exposure

AUTHOR(S): Short, S. C.; Mitchell, S. A.; Boulton, P.; Woodcock, M.; Joiner, M. C.

CORPORATE SOURCE: Mount Vernon Hospital, Gray Laboratory Cancer Research Trust, Middlesex, HA6 2JR, UK

SOURCE: International Journal of Radiation Biology (1999), 75(11), 1341-1348

CODEN: IJRBE7; ISSN: 0955-3002

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: To **examine** the low-dose radiation response of a series of radioresistant human glioma cell lines and determine if low-dose hypersensitivity is a characteristic of these cells. Materials and methods: The clonogenic survival of six radioresistant human glioma cell lines was measured following exposure to graded, single, very low doses of X-rays in vitro. High resolution was achieved using either a Dynamic Microscopic Image Processing Scanner (DMIPS) or a cell sorter (CS). Results: In five of the six cell lines tested, low-dose hypersensitivity (HRS) was demonstrated although in the sixth, a grade III astrocytoma line, it was not. These results are consistent with previous data indicating that low-dose hypersensitivity is more marked in more radioresistant cell lines although the difference between the glioblastoma cell lines with differing SF2 is not marked. Conclusion: Low-dose hypersensitivity is common in radioresistant glioma cell lines. This may have implications for the treatment of these tumors if further studies

confirm that HRS translates to increased effectiveness per Gy in vivo when very low doses per fraction are used.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:659383 HCAPLUS

DOCUMENT NUMBER: 131:271871

TITLE: Preparation of aminoalkyl-substituted
9H-pyridino[2,3-b]indole and 9H-pyrimidino[4,5-b]indole derivatives as CRF1 and NPY1 receptor antagonists

INVENTOR(S): Horvath, Raymond F.; Darrow, James W.;
Maynard, George D.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

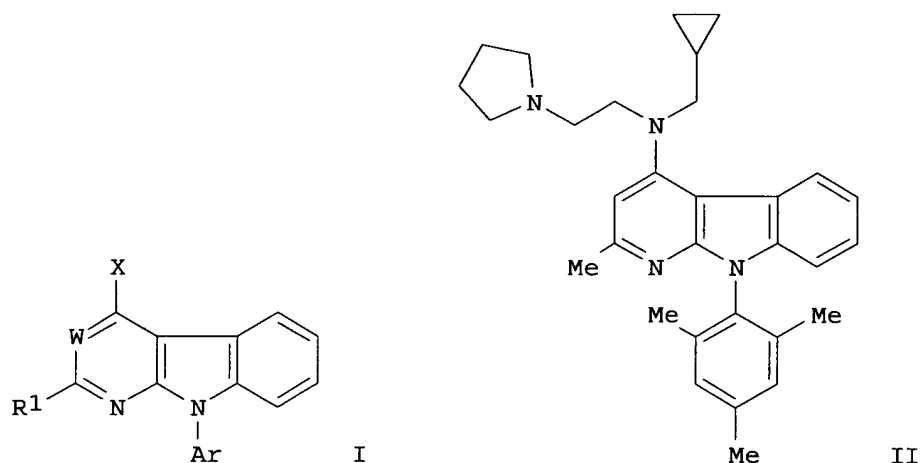
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|-------------------|----------|-----------------|--------------|
| WO 9951600 | A1 | 19991014 | WO 1999-US7254 | 19990401 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2326606 | AA | 19991014 | CA 1999-2326606 | 19990401 <-- |
| AU 9934645 | A1 | 19991025 | AU 1999-34645 | 19990401 <-- |
| EP 1068207 | A1 | 20010117 | EP 1999-916294 | 19990401 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-80451P | P 19980402 |
| | | | WO 1999-US7254 | W 19990401 |
| OTHER SOURCE(S): | MARPAT 131:271871 | | | |
| GI | | | | |



AB The title compds. I [where Ar = (un)substituted Ph, naphthyl, pyridyl, pyrimidinyl; R1 = H, halogen, CF₃, (hydroxy)alkyl, alkoxyalkyl, alkylthioalkyl; W = N, CH, or alkyl-substituted C; X = disubstituted amino] were prepared as corticotropin-releasing factor (CRF1) and neuropeptide Y (NPY1) receptor antagonists. For example, 2-amino-4,5,6,7-tetrahydro-1-(2,4,6-trimethylphenyl)-1H-indole-3-carbonitrile was formed by reaction of 2,4,6-trimethylaniline and adipoin in toluene followed by addition of malonitrile and ammonium acetate. The carbonitrile was cyclized with 2-methoxypropene in dichloroethane and reduced over Pd/C to yield the 4-amino-9H-pyridino[2,3-b]indole. Addition of cyclopropanecarbonyl chloride followed by ClCH₂COCl and pyrrolidine produced the disubstituted amino title compound II. The CRF1 receptor binding affinity for compds. of the invention was measured on membrane pellets containing CRF1 receptors and in IMR-32 cells; IC₅₀ values ranged from 0.5 nM to 10 μM and < 10 μM, resp. Invention compds. were assayed for NPY1 receptor binding activity using NPY Y1 receptors harvested from baculovirus-infected Sf9 cells and showed IC₅₀ values < 10 μM. The aminoalkyl-substituted 9H-pyridino[2,3-b]indole and 9H-pyrimidino[4,5-b]indole derivs. are claimed to be useful for the diagnosis and treatment of stress related disorders such as post traumatic stress disorder (PTSD), depression, headache, and anxiety, as well as a variety of clin. conditions characterized by the presence of an excess of neuropeptide Y.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:659381 HCAPLUS

DOCUMENT NUMBER: 131:286528

TITLE: Substituted 9H-pyridino[2,3-b]indole and 9H-pyrimidino[4,5-b]indole derivatives as selective neuropeptide Y receptor ligands

INVENTOR(S): Darrow, James W.; Maynard, George D.; Horvath, Raymond F.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

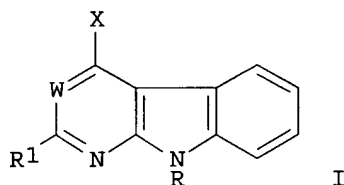
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|--------------|
| WO 9951598 | A1 | 19991014 | WO 1999-US7243 | 19990401 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9932202 | A1 | 19991025 | AU 1999-32202 | 19990401 <-- |
| US 6221875 | B1 | 20010424 | US 1999-283534 | 19990401 <-- |
| US 2001031758 | A1 | 20011018 | US 2001-841550 | 20010423 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-80423P | P 19980402 |
| | | | US 1999-283534 | A1 19990401 |
| | | | WO 1999-US7243 | W 19990401 |
| OTHER SOURCE(S): | | MARPAT 131:286528 | | |
| GI | | | | |



AB Title compds. I [R = (un)substituted Ph, naphthyl, pyridyl, pyrimidyl; R1 = H, halogen, CF3, alkyl, cycloalkylalkyl, cycloalkyl, hydroxyalkyl, alkoxyalkyl, mercaptoalkyl, alkylthioalkyl; W = N, CR2; R2 = H, alkyl; X = R3NH, R3O, R3S, R3SO2; R3 = (un)substituted aminoalkyl, aminoacyl] (122 compds.) are effective neuropeptide Y1 receptor antagonists (no data), and are therefore useful in the treatment of a wide variety of clin. conditions which are characterized by the presence of an excess of neuropeptide Y. The compds. are prepared by one of several different methods.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:659380 HCAPLUS

DOCUMENT NUMBER: 131:271870

TITLE: Preparation of aminoalkyl-substituted 5,6,7,8-tetrahydro-9H-pyridino[2,3-b]indole and 5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole derivatives as CRF1 specific ligands

INVENTOR(S): Horvath, Raymond F.; Darrow, James W.; Maynard, George D.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

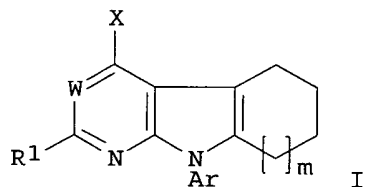
SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|--------------|
| WO 9951597 | A1 | 19991014 | WO 1999-US7122 | 19990401 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2326319 | AA | 19991014 | CA 1999-2326319 | 19990401 <-- |
| AU 9933759 | A1 | 19991025 | AU 1999-33759 | 19990401 <-- |
| EP 1068205 | A1 | 20010117 | EP 1999-915177 | 19990401 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002510686 | T2 | 20020409 | JP 2000-542318 | 19990401 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-80410P | P 19980402 |
| | | | WO 1999-US7122 | W 19990401 |
| OTHER SOURCE(S): | | | MARPAT 131:271870 | |
| GI | | | | |



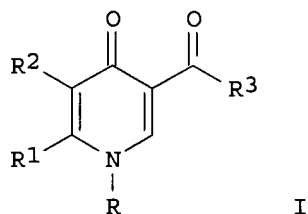
AB The title compds. I [Ar = Ph, 1- or 2-naphthyl, 5-pyrimidinyl, etc.; R1 = H, halo, CF3, etc.; W = N, CR3 with R3 = H, alkyl; m = 0-2; X = A1Y1V1NV2Y2A2], modulators of CRF receptors (no data), were prepared E.g., 4-(N-(2-pyrrolidinoethyl)-N-cyclopropylmethyl)amino-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyridino[2,3-b]indole was prepared

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1999:566032 HCAPLUS
 DOCUMENT NUMBER: 131:184869
 TITLE: Preparation of annelated 4-oxonicotiniccarboxamides as GABAA receptor ligands
 INVENTOR(S): Desimone, Robert W.; Rosewater, Daniel L.
 PATENT ASSIGNEE(S): Neurogen Corporation, USA
 SOURCE: PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|--------------|
| WO 9943661 | A2 | 19990902 | WO 1999-US4310 | 19990226 <-- |
| WO 9943661 | A3 | 20000106 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2322167 | AA | 19990902 | CA 1999-2322167 | 19990226 <-- |
| AU 9927940 | A1 | 19990915 | AU 1999-27940 | 19990226 <-- |
| EP 1056724 | A2 | 20001206 | EP 1999-908533 | 19990226 <-- |
| EP 1056724 | B1 | 20050525 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 6194427 | B1 | 20010227 | US 1999-259244 | 19990226 <-- |
| JP 2002504544 | T2 | 20020212 | JP 2000-533418 | 19990226 <-- |
| AT 296290 | E | 20050615 | AT 1999-908533 | 19990226 |
| ES 2243046 | T3 | 20051116 | ES 1999-908533 | 19990226 |
| BR 9908321 | A | 20011218 | BR 1999-8321 | 19990926 <-- |
| US 6448259 | B1 | 20020910 | US 2000-565531 | 20000505 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-76022P | P 19980226 |
| | | | US 1999-259244 | A1 19990226 |
| | | | WO 1999-US4310 | W 19990226 |
| OTHER SOURCE(S): | | | MARPAT 131:184869 | |
| GI | | | | |

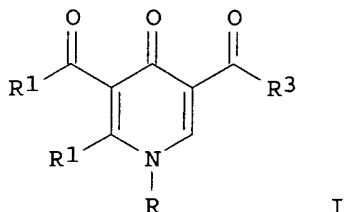


AB Title compds. [I; R = H, OH, alkyl; R1R2 = atoms to complete an (un)substituted carbocyclic ring; R3 = NHR4; R4 = (ar)alkyl, (hetero)aryl, etc] were prepared. Thus, I [R = H, R1R2 = (CH2)3] (II; R3 = OH) was amidated by 4-(MeO)C6H4CH2NH2 to give II [R3 = NHCH2C6H4(OMe)-4]. Data for biol. activity of I were given.

L18 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1999:566031 HCAPLUS
 DOCUMENT NUMBER: 131:184868
 TITLE: Preparation of alkanoyloxonicotiniccarboxamides and analogs as GABAA receptor ligands
 INVENTOR(S): Desimone, Robert W.; Manly, Charles
 PATENT ASSIGNEE(S): Neurogen Corporation, USA
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|--------------|
| WO 9943660 | A1 | 19990902 | WO 1999-US4303 | 19990226 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9928811 | A1 | 19990915 | AU 1999-28811 | 19990226 <-- |
| US 6156898 | A | 20001205 | US 1999-258836 | 19990226 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-76023P | P 19980226 |
| | | | WO 1999-US4303 | W 19990226 |
| OTHER SOURCE(S): | | MARPAT 131:184868 | | |
| GI | | | | |



AB Title compds. [I; R = H or alkyl; R1 = alkyl; R2 = H or alkyl; R1R2 = (un)substituted (CH2)2-4; R3 = NHR4; R4 = (ar)alkyl, (hetero)aryl, etc] were prepared Thus, I [R = H, R1 = R2 = Me] (II; R3 = OH) was amidated by 4-methyl-2-aminothiazole to give II [R3 = 4-methyl-2-thiazolylamino]. Data for biol. activity of I were given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:511160 HCAPLUS

DOCUMENT NUMBER: 131:144604

TITLE: Preparation of **oxodipyridoimidazole**

-carboxamides: GABAa brain receptor ligands
 INVENTOR(S): Xie, Linghong; Currie, Kevin S.; Albaugh, Pamela; Shaw, Kenneth; Hutchison, Alan J.

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 186 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

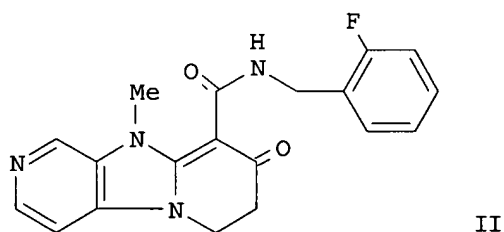
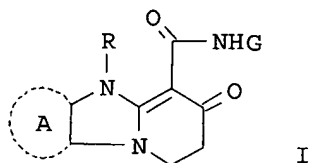
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

WO 9940092 A1 19990812 WO 1999-US1688 19990204 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9926534 A1 19990823 AU 1999-26534 19990204 <--
PRIORITY APPLN. INFO.: US 1998-18754 A 19980204
OTHER SOURCE(S): MARPAT 131:144604 WO 1999-US1688 W 19990204
GI



AB Title compds. [I; A represents an optionally substituted nitrogen-containing ring system; R is H, alkyl cycloalkyl, arylalkyl, heteroarylalkyl; G, an organic or inorg. group, is cycloalkyl, alkyl, etc.], stereoisomers, and pharmaceutically acceptable salts thereof are prepared and are highly selective agonists, antagonists or inverse agonists for GABA_A brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABA_A brain receptors, and are therefore useful in the diagnosis and treatment of anxiety, Down Syndrome, sleep, cognitive and seizure disorders, depression, overdose with benzodiazepine drugs and for enhancement of alertness. Thus, the title compound II, tested on rat cortical tissue, was prepared from reduction, cyclizaion of 4-chloro-3-nitropyridine, Et 3-aminopropionate, Et 3-amino-3-ethoxyacrylate hydrochloride, 2-fluorobenzylamine, and methylation by Me iodide.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:438530 HCAPLUS

DOCUMENT NUMBER: 131:241366
TITLE: **Trimethylamine** and foetor hepaticus
AUTHOR(S): **Mitchell, S.**; Ayesh, R.; Barrett, T.; Smith, R.
CORPORATE SOURCE: Molecular Toxicology, Division of Biomedical Sciences, Imperial College School of Medicine, London, UK
SOURCE: Scandinavian Journal of Gastroenterology (1999), 34(5), 524-528
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Scandinavian University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: In patients with various degrees of hepatocellular failure and portosystemic shunting of blood, the breath may acquire a sweet, musty, or even slightly fecal aroma, termed foetor hepaticus, which has been attributed mainly to volatile sulfur compds. with contributions from various nitrogenous substances. Not infrequently in such patients, unusual body odors are also encountered and, by analogy with the 'fish-odor syndrome' known to be caused by excessive **trimethylamine**, the availability of this latter graveolent **amine** to potentially contribute to odors associated with hepatic disease was investigated. Methods: Urine (0-24 h) was collected from 63 patients with various liver diseases previously confirmed in hospital by means of various biochem., immunol., pathol., and radiol. investigations. Total **trimethylamine** and **trimethylamine** N-oxide levels in urine were measured with head-space gas chromatog. Results: In total, 50% (32 of 63) of the patients (primary liver disease, 25 of 47, or 53.2%; secondary liver disease, 7 of 16, or 43.8%) had urinary **trimethylamine** levels greater than the upper end of the range considered normal (0.08-1.84 µg/mL). Seventeen patients excreted large amts. of free **trimethylamine** (more than 10 µg/mL), above the threshold usually associated with the appearance of a 'fish-like' body odor and tainted breath. Conclusions: Excessive amts. of **trimethylamine** may well contribute to the overall body odor problems encountered among patients with severe hepatic disease, precipitating in

these individuals a secondary form of the 'fish-odor syndrome'.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:166616 HCAPLUS
DOCUMENT NUMBER: 130:196645
TITLE: Preparation of 4-oxonaphthyridine-3-carboxamides as GABA brain receptor ligands
INVENTOR(S): Albaugh, Pamela; **Desimone, Robert W.**; Liu, Gang
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 9910347 | A1 | 19990304 | WO 1998-US17513 | 19980824 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, | | | | |

KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

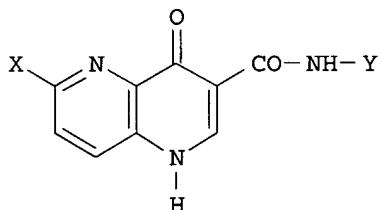
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|--|----|----------|------------------|--------------|
| CA 2301599 | AA | 19990304 | CA 1998-2301599 | 19980824 <-- |
| CA 2301599 | C | 20030325 | | |
| AU 9891173 | A1 | 19990316 | AU 1998-91173 | 19980824 <-- |
| AU 753800 | B2 | 20021031 | | |
| EP 1007526 | A1 | 20000614 | EP 1998-943352 | 19980824 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9811362 | A | 20000822 | BR 1998-11362 | 19980824 <-- |
| SI 20270 | C | 20001231 | SI 1998-20055 | 19980824 <-- |
| JP 2001514181 | T2 | 20010911 | JP 2000-507675 | 19980824 <-- |
| EG 21717 | A | 20020227 | EG 1998-1180 | 19980929 <-- |
| TW 574221 | B | 20040201 | TW 1998-87117597 | 19981023 |
| MX 200001598 | A | 20001026 | MX 2000-1598 | 20000215 <-- |
| NO 2000000822 | A | 20000413 | NO 2000-822 | 20000218 <-- |
| BG 104192 | A | 20010531 | BG 2000-104192 | 20000225 <-- |
| LV 12539 | B | 20010120 | LV 2000-29 | 20000316 <-- |

PRIORITY APPLN. INFO.:

US 1997-918180 A 19970825
 WO 1998-US17513 W 19980824

OTHER SOURCE(S): MARPAT 130:196645

GI



AB The title compds. I [X is hydrogen, halogen, (un)substituted alkyl, (un)substituted alkoxy or amino; and Y is (un)substituted alkyl, aryl, or heteroaryl] are prepared. I are highly selective agonists, antagonists or inverse agonists for GABA_A brain receptors or prodrugs of agonists, antagonists or inverse agonists for GABA_A brain receptors. These compds. are useful in the diagnosis and treatment of anxiety, Down Syndrome, sleep, cognitive and seizure disorders, and overdose with benzodiazepine drugs and for enhancement of alertness. In in vitro assays for GABA_A receptor activity using rat cortical tissue homogenate and 3H-Flumazenil and diazepam, compds. of this invention showed K_i values of less than 1 μM.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

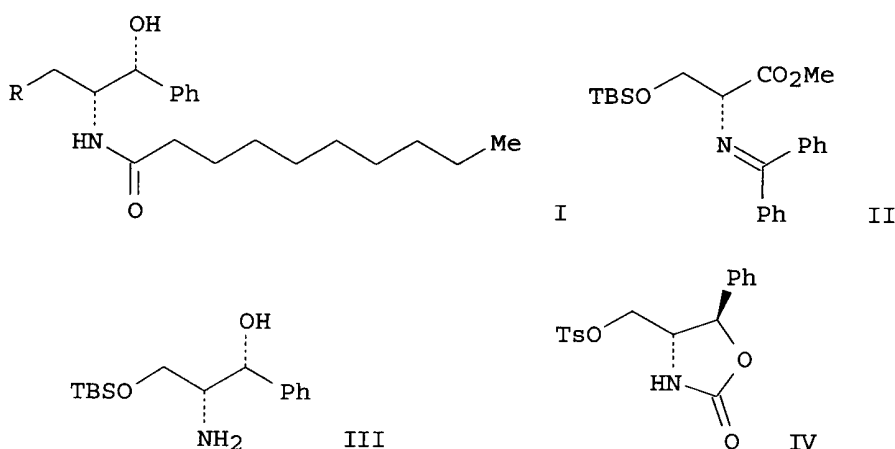
L18 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:701626 HCAPLUS

DOCUMENT NUMBER: 130:81805

TITLE: Glycosyltransferase Inhibitors: Synthesis of
 D-threo-PDMP, L-threo-PDMP, and Other Brain
 Glucosylceramide Synthase Inhibitors from D- or
 L-Serine

AUTHOR(S): Mitchell, Scott A.; Oates, Bryan D.; Razavi, Hossein; Polt, Robin
 CORPORATE SOURCE: Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA
 SOURCE: Journal of Organic Chemistry (1998), 63(24), 8837-8842
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 130:81805
 GI



AB The synthesis of enantiomerically pure (1S,2S)-1-phenyl-2-decanoylamino-3-N-morpholino-1-propanol (L-threo-PDMP) from L-serine, and the enantiomer (1R,2R)-1-phenyl-2-decanoylamino-3-morpholino-1-propanol (D-threo-PDMP) (I; R = morpholino) from D-serine is reported. Reductive alkylation of the fully protected O'Donnell's Schiff base (II) derived from D-serine provided the β -amino alc. III in high yield and excellent selectivity, which yielded optically pure I (R = morpholino) in high yield after six steps. Three other D-threo-PDMP analogs I (R = thiomorpholino, piperidino, pyrrolidino) with various **amine** groups have been synthesized using the same methodol., including the more potent pyrrolidine compound. A key feature of the synthesis is the isolation of tosylate IV, which allows for the divergent synthesis of many analogs from a common advanced intermediate. The synthesis is amenable to large-scale production of D-threo-PDMP, L-threo-PDMP, and similar compds.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

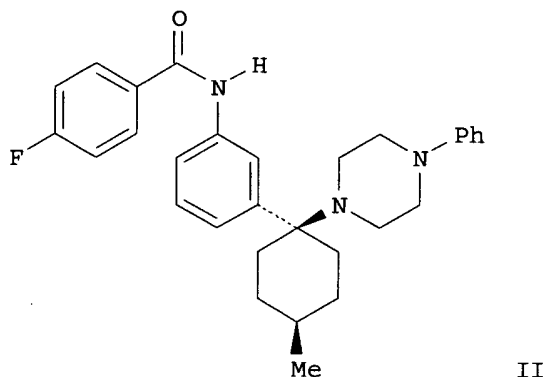
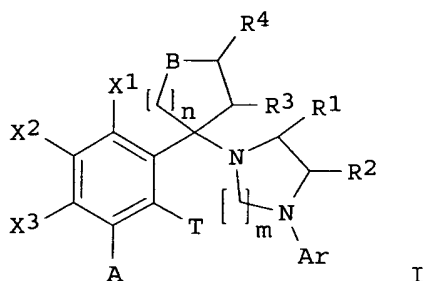
ACCESSION NUMBER: 1998:87721 HCAPLUS

DOCUMENT NUMBER: 128:154099

TITLE: Preparation of amido- and amino-substituted **benzylamine** derivatives such as amides of cis-1-(3-aminophenyl)-1-(4-phenyl-1-piperazinyl)-4-methylcyclohexane as a new class of neuropeptide Y1 specific ligands

INVENTOR(S): Blum, Charles A.; **Desimone, Robert**;
 Hutchison, Alan; Peterson, John
 PATENT ASSIGNEE(S): Neurogen Corp., USA
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|--------------|
| WO 9803494 | A1 | 19980129 | WO 1997-US12690 | 19970718 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2260983 | AA | 19980129 | CA 1997-2260983 | 19970718 <-- |
| AU 9736718 | A1 | 19980210 | AU 1997-36718 | 19970718 <-- |
| EP 918761 | A1 | 19990602 | EP 1997-933564 | 19970718 <-- |
| EP 918761 | B1 | 20030502 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6133265 | A | 20001017 | US 1997-897046 | 19970718 <-- |
| JP 2000515527 | T2 | 20001121 | JP 1998-507143 | 19970718 <-- |
| AT 239002 | E | 20030515 | AT 1997-933564 | 19970718 <-- |
| PT 918761 | T | 20030930 | PT 1997-933564 | 19970718 |
| ES 2197354 | T3 | 20040101 | ES 1997-933564 | 19970718 |
| ZA 9706470 | A | 19980804 | ZA 1997-6470 | 19970722 <-- |
| MX 9900869 | A | 20000331 | MX 1999-869 | 19990122 <-- |
| US 6316617 | B1 | 20011113 | US 2000-633055 | 20000808 <-- |
| PRIORITY APPLN. INFO.: | | | US 1996-22298P | P 19960723 |
| | | | US 1997-897046 | A1 19970718 |
| | | | WO 1997-US12690 | W 19970718 |
| OTHER SOURCE(S): | | | MARPAT 128:154099 | |
| GI | | | | |



AB The title compds. [I; one of X1, X2, X3 = -Q(D)C(:E)(CH₂)_oG, -Q(D)SO₂(CH₂)_oG and the remaining X1, X2, X3 = H; Q = N, O; D is absent when Q = O and when Q = N; D = H, C1-6 alkyl; DG = may form a ring; E = O, H₂; o = 0-1; G = C1-6 alkyl; (un)substituted aryl; (un)substituted heteroaryl, etc.; Ar = (un)substituted Ph, pyridyl, thienyl, etc.; B = S, O, N(R5), C(R5)(R6); n = 1-3; m = 2-4; A, T = H, halo, OH, etc.; R1, R2 = H, C1-6 alkyl; R3, R4 = H, C1-6 alkyl, C1-6 alkoxy; R5 = H, C1-6 alkyl, Ph, pyridyl; R6 = H, OH, NH₂, etc.], useful in the diagnosis and treatment of feeding disorders such as obesity and bulimia and cardiovascular diseases such as essential hypertension and congestive heart failure due to the binding of these compds. to human neuropeptide Y1 receptors, were prepared. Thus, reaction of cis-1-(3-aminophenyl)-1-(4-phenylpiperazin-1-yl)-4-methylcyclohexane (preparation described) with 4-fluorobenzoyl chloride in the presence of 4-dimethylaminopyridine in pyridine afforded the title compound cis-II. Compds. I are effective at 0.1-140 mg/kg/day.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:439245 HCAPLUS

DOCUMENT NUMBER: 127:95137

TITLE: Singlet oxygen in synthesis. Formation of d,l- and meso-Isochrysohermidin from a 3,3'-bipyrrrole precursor

AUTHOR(S): Wasserman, Harry H.; Rotello, Vincent M.; Frechette, Roger; Desimone, Robert W.; Yoo, Ji Uk; Baldino, Carmen M.

CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA

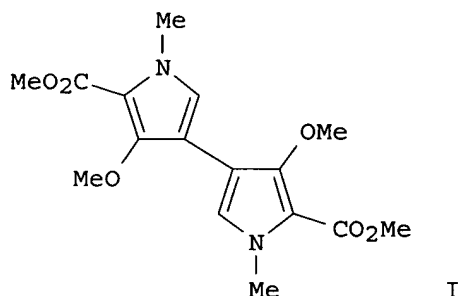
SOURCE: Tetrahedron (1997), 53(26), 8731-8738

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 127:95137
 GI



AB A synthesis of the d,l and meso forms of isochrysohermidin is outlined which employs the singlet oxygen oxidation of pyrroles as the key step. The bipyrrole precursor I was synthesized from a 3-hydroxy monopyrrole which, in turn, was prepared by addition of **methylamine** to a vinyl vicinal tricarbonyl.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:121338 HCAPLUS

DOCUMENT NUMBER: 126:131456

TITLE: Preparation of **N-benzazolylylbenzimidazolones** and related compounds as GABAA brain receptor ligands.

INVENTOR(S): **Desimone, Robert W.**; Blum, Charles A.

PATENT ASSIGNEE(S): Neurogen Corporation, USA; Desimone, Robert W.; Blum, Charles A.

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

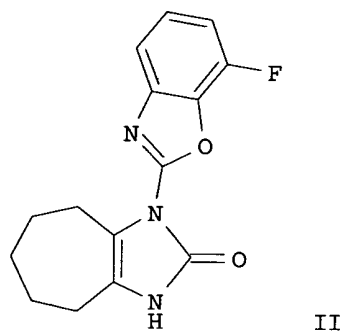
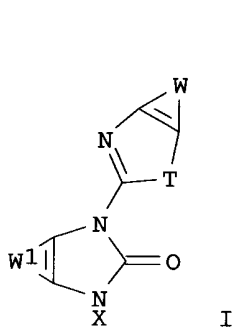
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 9639404 | A1 | 19961212 | WO 1996-US10214 | 19960604 <-- |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM | | | | |
| US 5637724 | A | 19970610 | US 1995-461641 | 19950605 <-- |
| US 5637725 | A | 19970610 | US 1995-462674 | 19950605 <-- |
| CA 2223936 | AA | 19961212 | CA 1996-2223936 | 19960604 <-- |
| CA 2223936 | C | 20040120 | | |
| AU 9661743 | A1 | 19961224 | AU 1996-61743 | 19960604 <-- |
| AU 717630 | B2 | 20000330 | | |
| EP 830359 | A1 | 19980325 | EP 1996-919393 | 19960604 <-- |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI

| | | | | |
|------------------------|-------------------|----------|-----------------|--------------|
| US 5849927 | A | 19981215 | US 1997-872542 | 19970610 <-- |
| US 5936095 | A | 19990810 | US 1997-872242 | 19970610 <-- |
| US 6127395 | A | 20001003 | US 1999-368301 | 19990803 <-- |
| PRIORITY APPLN. INFO.: | | | US 1995-461641 | A2 19950605 |
| | | | US 1995-462674 | A 19950605 |
| | | | WO 1996-US10214 | W 19960604 |
| | | | US 1997-872242 | A1 19970610 |
| OTHER SOURCE(S): | MARPAT 126:131456 | | | |
| GI | | | | |



AB Title compds. [I; T = NH, O, S; X = H, OH, alkyl, (substituted) amide; W = atoms to complete a (substituted) benzo, thieno, or pyrido ring; W1 = atoms to complete a (substituted) benzene or cycloalkyl ring; n = 0-3; R3-R6 = H, halo, substituted alkyl, alkoxy, Ph, pyridyl, phenylalkyl, pyridylalkyl; R7-R10 = H, alkyl; R7R8 = (CH2)m; m = 2-4], were prepared Thus, title compound (II) bound to GABAA receptors with $K_i = 3.0$ nM.

L18 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:232385 HCAPLUS

DOCUMENT NUMBER: 124:281488

TITLE: 6-OHDA lesions of the nucleus accumbens accentuate memory deficits in animals with lesions to the forebrain cholinergic projection system: effects of nicotine administration on learning and memory in the water maze

AUTHOR(S): Grigoryan, G.; Hodges, H.; **Mitchell, S.**;
Sinden, J. D.; Gray, J. A.

CORPORATE SOURCE: Department of Psychology, Institute of Psychiatry,
London, SE5 8AF, UK

SOURCE: Neurobiology of Learning and Memory (1996),
65(2), 135-53

CODEN: NLMEFR; ISSN: 1074-7427

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The sep. and combined effects of lesions to the forebrain cholinergic projection system (FCPS) and to dopamine (DA) terminals in the nucleus accumbens (n.acc) were assessed in two water maze tasks: (1) standard acquisition using two trials/day with a 10 min intertrial interval (ITI) for 15 days with the platform in the same position and (2) a working memory task requiring matching to a platform position located by chance on Trial 1, with four trials/day separated by a 30-s ITI and a different platform

position on each of 4 days. Effects of nicotine (0.1 mg/kg) were also examined in animals with FCPS, n.acc, and combined lesions to determine whether facilitatory effects of nicotine in FCPS lesioned animals are mediated by **dopamine** release in the n.acc. The FCPS and combined lesion groups were impaired in both tasks, but the combined lesion group was substantially worse than animals with FCPS lesions alone. The n.acc lesion group did not differ from controls. Nicotine did not affect acquisition in either the FCPS or combined lesion group, but impaired learning in animals with n.acc lesions. In the working memory task nicotine exerted a nonspecific facilitatory effect in the FCPS and combined lesion groups, by reducing latency to find the platform both on the first trial and on the subsequent matching to position trials. Choline acetyltransferase (ChAT) activity was reduced in hippocampus and cortex in the FCPS lesion group, whereas DA levels in n.acc were increased. Conversely, in the n.acc lesion group accumbal DA levels were reduced, while cortical and hippocampal ChAT activity was increased, suggesting that reciprocal changes were induced by the sep. lesions. However the combined lesion group showed mixed and more widespread effects; ChAT activity was unaltered in cortex and substantially reduced in hippocampus, and DA levels were reduced in both n.acc and caudate. The results indicate that combined FCPS and n.acc lesions impair spatial learning and working memory far more severely than FCPS lesions alone, although this does not reflect simple additive redns. in DA and ChAT activity. Nicotine improved spatial search strategy, an effect detected in the working memory task with daily changes in platform position, rather than in the standard acquisition task, but did not appear specifically to improve working memory. Since the facilitatory effect of nicotine was seen in both FCPS and combined lesion groups, the findings suggest that nicotine-induced improvements do not depend on accumbal DA release.

L18 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:797773 HCAPLUS
 DOCUMENT NUMBER: 123:338891
 TITLE: Singlet Oxygen Reactions from the Adducts of Ozone with Heterocyclic Substrates
 AUTHOR(S): Wasserman, Harry H.; Yoo, Ji Uk; **DeSimone, Robert W.**
 CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
 SOURCE: Journal of the American Chemical Society (1995), 117(38), 9772-3
 CODEN: JACSAT; ISSN: 0002-7863
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

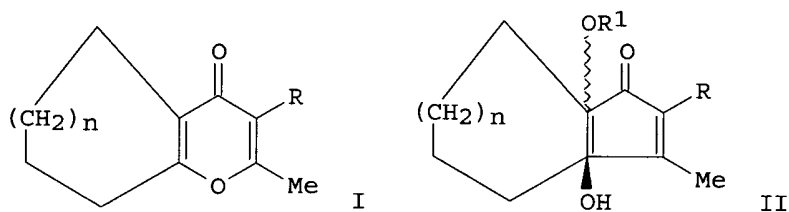
AB Ozone in dilute concentration reacts with heterocyclic systems such as pyrroles, oxazoles and **imidazoles** at low temps. to form adducts which, on warming, form monooxygenation products of the hetero system and at the same time release singlet oxygen. The singlet oxygen may react with the parent heterocyclic system, or may be captured by other typical singlet oxygen acceptors.

L18 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:760033 HCAPLUS
 TITLE: Neuropsychology: Is **dopamine** a missing link?
 AUTHOR(S): **Desimone, Robert**
 CORPORATE SOURCE: Lab. Neuropsychology, Natl. Inst. Mental Health, Bethesda, MD, 20892-4415, USA
 SOURCE: Nature (London) (1995), 376(6541), 549-50

PUBLISHER: CODEN: NATUAS; ISSN: 0028-0836
 DOCUMENT TYPE: Macmillan Magazines
 LANGUAGE: Journal; News Announcement
 English
 AB Unavailable

L18 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1994:163507 HCAPLUS
 DOCUMENT NUMBER: 120:163507
 TITLE: Photochemical ring contraction of fused bicyclic
 4-pyrones: a novel 2-step cyclopentannulation approach
 AUTHOR(S): West, F. G.; Fisher, P. V.; Gunawardena, G. U.;
Mitchell, Scott
 CORPORATE SOURCE: Dep. Chem., Univ. Utah, Salt Lake City, UT, 84112, USA
 SOURCE: Tetrahedron Letters (1993), 34(29), 4583-6
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 120:163507
 GI



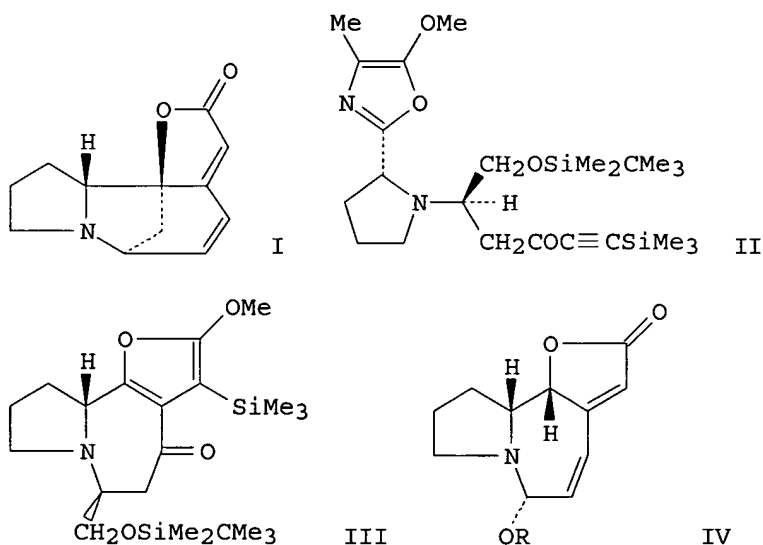
AB Fused bicyclic 4-pyrones I ($n = 0, 2$, $R = H$; $n = 1$, $R = H$, PhCH_2 ; $n = 3$, $R = H$, Me) were prepared by condensation of **enamines** derived from cyclic ketones with diketene or substituted 1,3-dioxin-4-ones. Photolysis of I ($n = 1-3$) in a hydroxylic medium led to bicyclo[n.3.0]alkenones II ($R_1 = H$, Me) bearing oxygenation at both angular positions. This process occurs via regioselective nucleophilic solvent attack on the intermediate tricyclic oxyallyl zwitterion. The efficiency of the transformation depends on the size of the ring fused to the 4-pyrone.

L18 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1993:183296 HCAPLUS
 DOCUMENT NUMBER: 118:183296
 TITLE: **Scopolamine** affects short-term memory but
 not inferior temporal neurons
 AUTHOR(S): Miller, Earl K.; **Desimone, Robert**
 CORPORATE SOURCE: Lab. Neuropsychol., Natl. Inst. Ment. Health,
 Bethesda, MD, USA
 SOURCE: NeuroReport (1993), 4(1), 81-4
 CODEN: NERPEZ; ISSN: 0959-4965
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Effects of **scopolamine** on performance of a delayed matching-to-sample task and on the properties of neurons in anterior-ventral inferior temporal (IT) cortex were examined in two monkeys. Both monkeys were impaired on the task after systemic administration of **scopolamine**, suggesting that **scopolamine** disrupts recent memory. Despite the behavioral deficit, neurons in IT cortex, a

region having an important role in visual memory and neuronal properties consistent with that role, were largely unaffected by **scopolamine**. This dissociation between the behavioral and neuronal effects of **scopolamine** indicates that the drug either acts at a different site or disrupts unobsd. mechanisms at the IT site.

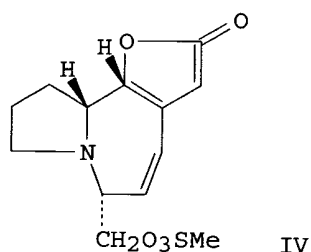
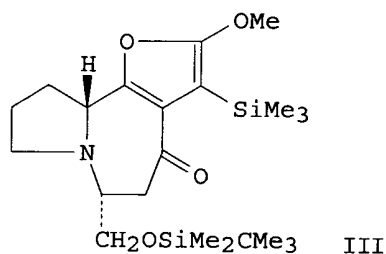
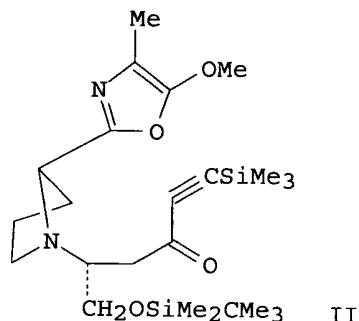
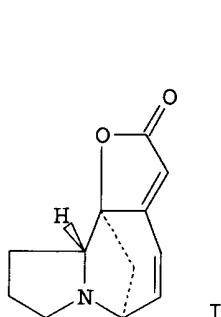
L18 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1991:514830 HCAPLUS
 DOCUMENT NUMBER: 115:114830
 TITLE: Bis-heteroannulation. 15. Enantiospecific syntheses of (+)- and (-)-norsecurinine
 AUTHOR(S): Jacobi, Peter A.; Blum, Charles A.; DeSimone, Robert W.; Udodong, Uko E. S.
 CORPORATE SOURCE: Hall-Atwater Lab., Wesleyan Univ., Middletown, CT, 06457, USA
 SOURCE: Journal of the American Chemical Society (1991), 113(14), 5384-92
 CODEN: JACSAT; ISSN: 0002-7863
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 115:114830
 GI



AB (-)-Norsecurinine (I) was prepared in a stereospecific fashion with the acetylenic oxazole II as the starting material. Diels-Alder cyclization of II afforded the furano ketone III, which was transformed in five steps to the butenolide mesylate IV (R = MeSO₂). Transannular alkylation of IV (R = MeSO₂) then afforded I. In identical fashion, ent-II gave (+)-norsecurinine. The structure of ent-IV (R = H) was determined by x-ray anal.

L18 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1990:497872 HCAPLUS
 DOCUMENT NUMBER: 113:97872
 TITLE: Total synthesis of (+)- and (-)-norsecurinine
 AUTHOR(S): Jacobi, Peter A.; Blum, Charles A.; DeSimone, Robert W.; Udodong, Uko E. S.

CORPORATE SOURCE: Hall-Atwater Lab., Wesleyan Univ., Middletown, CT,
06457, USA
SOURCE: Tetrahedron Letters (1989), 30(51), 7173-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:97872
GI



AB (-)-Norsecurinine (I) was prepared in a stereospecific fashion beginning with the acetylenic oxazole II. Diels-Alder cyclization of II afforded the furanoketone III, which was transformed in five steps to the butenolide mesylate IV. Transannular alkylation of IV then afforded I. In identical fashion, ent-II gave (+)-norsecurinine.

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